1: Antisense Res Dev. 1993 Winter;3(4):323-38.

Inhibition of HIV-1 replication in cultured cells with antisense oligonucleotides encapsulated in immunoliposomes.

Zelphati O, Zon G, Leserman L.

Centre d'Immunologie, Institut National de la Sante et de la Recherche Medicale-Centre National de la Recherche Scientifique de Marseille-Luminy, France.

Antisense oligonucleotides inhibit HIV replication in vitro, but their activity is limited by their sensitivity to nucleases and low cellular uptake. To see whether these problems could be circumvented, we compared effects of HIV-1 rev and tat gene-specific antisense phosphodiester or phosphorothioate oligonucleotides, either free in solution or encapsulated in antibody-targeted liposomes (immunoliposomes), on acutely or chronically infected cells. Phosphodiester antisense oligonucleotides were inactive in their free form in acutely and chronically infected cells (up to a concentration of 50 microM). When encapsulated in immunoliposomes directed to HLA class I molecules expressed by targeted cells, they inhibited viral replication (at a concentration of 0.5 microM) in acutely infected cells in a sequence-specific manner. The same phosphodiester antisense oligonucleotides in liposomes had no antiviral activity in chronically infected cells. In acutely infected cells, phosphorothioate oligonucleotides free in solution inhibited the replication of HIV without sequence specificity and had slightly greater activity, also nonspecific, when encapsulated in liposomes. Phosphorothioate antisense (anti-rev) oligonucleotides specifically blocked HIV replication in chronically infected cells. When encapsulated in targeted liposomes the efficiency of inhibition for these cells was increased by at least 60-fold relative to the same oligonucleotide free in solution.

PMID: 8155974 [PubMed - indexed for MEDLINE]

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                                                 ENTRY     SESSION
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=> s lipsome conjugate
L1             0 LIPSOME CONJUGATE

=> s liposome conjugate
L2           304 LIPOSOME CONJUGATE

=> s l2 and anti-CD4
L3             0 L2 AND ANTI-CD4

=> s l2 and HLA
L4             1 L2 AND HLA

=> d l4 cbib abs

L4   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2004 ACS on STN
1999:119837  Document No. 130:195756  Conjugates of polymers and antibodies
     specific for T lymphocytes, and their use as adjuvants.  Chang, Tse Wen
     (Tanox Biosystems, Inc., USA).  U.S. US 5872222 A  19990216, 6 pp.,
     Cont.-in-part of U.S. Ser. No. 926.566, abandoned.  (English).  CODEN:
     USXXAM.  APPLICATION: US 1992-993291 19921218.  PRIORITY: US 1991-688000
     19910419; US 1992-819449 19920110; US 1992-926566 19920806.
AB   Disclosed are conjugates including a substantially nonimmunogenic polymer
     backbone or microbead and binding mols., such as Fv, Fab, or F(ab')2
     fragments of monoclonal antibodies or whole antibodies that are bound
     through their Fc carbohydrate moieties or have their Fc portion modified
     so that they cannot effect ADCC (antibody-dependent cellular cytotoxicity)
     or complement-mediated cytolysis, and that are specific for a T cell
     surface antigen, such as CD3, TCR, CD4, CD8, or CD28 on T cells.  The
     polymer or microbead is preferably made of cross-linked dextran, ficoll,
     latex, or agarose, and is preferably of 0.1 to 10 μm in size, so that
     it can be suspended in fluids for in vivo applications.  These conjugates
     can be used as adjuvants to enhance the antibody response against an
     administered immunogen.
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=> s HLA-DR antibod?
L5          880 HLA-DR ANTIBOD?

=> s l5 and conjugated liposome
L6            0 L5 AND CONJUGATED LIPOSOME

=> s l5 and conjugate
L7            8 L5 AND CONJUGATE

=> s l7 and liposome
L8            2 L7 AND LIPOSOME

=> dup remove l8
PROCESSING COMPLETED FOR L8
L9            2 DUP REMOVE L8 (0 DUPLICATES REMOVED)

=> d l9 1-2 cbib abs

L9   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2004 ACS on STN
2002:4988   Document No. 137:174682  Targeted delivery of indinavir to HIV-1
     primary reservoirs with immunoliposomes.  Gagne, Jean-Francois;
     Desormeaux, Andre; Perron, Sylvie; Tremblay, Michel J.; Bergeron, Michel
     G. (Centre de Recherche en Infectiologie, Universite Laval, Centre
     Hospitalier Universitaire de Quebec, Quebec, QC, Can.).  Biochimica et
     Biophysica Acta, 1558(2), 198-210 (English) 2002.  CODEN: BBACAQ.  ISSN:
     0006-3002.  Publisher: Elsevier Science B.V..
AB   The tissue distribution of indinavir, free or incorporated into sterically
     stabilized anti-HLA-DR immunoliposomes, has been evaluated after a single
     s.c. injection to C3H mice.  Administration of free indinavir resulted in
     low drug levels in lymphoid organs.  In contrast, sterically stabilized
     anti-HLA-DR immunoliposomes were very efficient in delivering high concns.
     of indinavir to lymphoid tissues for at least 15 days post-injection
     increasing by up to 126 times the drug accumulation in lymph nodes.  The
     efficacy of free and immunoliposomal indinavir has been evaluated in
     vitro.  Results showed that immunoliposomal indinavir was as efficient as
     the free agent to inhibit HIV-1 replication in cultured cells.  The
     toxicity and immunogenicity of repeated administrations of liposomal
     formulations have also been investigated in rodents.  No significant
     differences in the levels of hepatic enzymes of mice treated with free or
     liposomal indinavir were observed when compared to baseline and control
     untreated mice.  Furthermore, histopathol. studies revealed no significant
     damage to liver and spleen when compared to the control group.
     Liposomes bearing Fab' fragments were 2.3-fold less immunogenic
     than liposomes bearing the entire IgG.  Incorporation of
     antiviral agents into sterically stabilized immunoliposomes could
     represent a novel therapeutic strategy to target specifically HIV
     reservoirs and treat more efficiently this retroviral infection.

L9   ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2004 ACS on STN
1998:486512   Document No. 129:184814  A novel method of cell-specific mRNA
     transfection.  Sawai, Keisuke; Ohno, Kouichi; Iijima, Yasushi; Levin,
     Brandi; Meruelo, Daniel (Department of Pathology and Kaplan Cancer Center,
     New York University Medical Center, New York, NY, 10016, USA).  Molecular
     Genetics and Metabolism, 64(1), 44-51 (English) 1998.  CODEN: MGMEFF.
     ISSN: 1096-7192.  Publisher: Academic Press.
AB   In this study, we developed a cell-specific mRNA transfection system using
     streptavidin-protein A (ST-PA) fusion protein and monoclonal antibodies
     (mAbs).  We previously reported that ST-PA fusion protein and mAb
     complexes can transfer certain biotinylated proteins into specific cell
     types.  At this time, we combined an in vitro transcribed biotinylated and
     self-replicating Sindbis virus genomic RNA with ST-PA fusion protein and
     mAbs.  In the presence of cationic liposomes, to prevent RNA
     degradation, this complex is able to transfect a reporter gene to specific
```

cancer cells in a mAb dose-dependent manner. Even in the absence of cationic **liposomes**, biotinylated mRNA, ST-PA fusion, and mAb complexes can transfer some types of cancer cell suspension cultures. This cell-specific transfection system is a novel method of introducing various mRNAs into cells that results in high levels of transient protein expression. (c) 1998 Academic Press.

=> s l2 and conjugate
L10 304 L2 AND CONJUGATE

=> s l10 and CD4
L11 18 L10 AND CD4

=> dup remove l11
PROCESSING COMPLETED FOR L11
L12 7 DUP REMOVE L11 (11 DUPLICATES REMOVED)

=> d l12 1-7 cbib abs

L12 ANSWER 1 OF 7 MEDLINE on STN DUPLICATE 1
2003247355. PubMed ID: 12769784. Surface-linked liposomal antigen induces IgE selective unresponsiveness in a T-cell independent fashion. Uchida Tetsuya. (Department of Safety Research on Blood and Biological Products, National Institute of Infectious Diseases, Musashimurayama-city, Tokyo, Japan.. tuchida@nih.go.jp) . Current drug targets. Immune, endocrine and metabolic disorders, (2003 Jun) 3 (2) 119-35. Ref: 58. Journal code: 101121150. ISSN: 1568-0088. Pub. country: Netherlands. Language: English.
AB We previously reported that surface-linked liposomal antigen induced IgE-selective unresponsiveness. The results were consistent even when different coupling procedures for antigen with liposomes, or for liposomes with different lipid components, were employed. During the course of an investigation intended to clarify the mechanism of IgE-selective unresponsiveness induced by surface-coupled liposomal antigens, we discovered an alternative approach to regulate the production of IgE, one that is independent of the activity of T-cells. Immunization of mice with OVA-**liposome conjugates** induced IgE- selective unresponsiveness without apparent Th1 polarization. Neither interleukin-12 (IL-12), IL-10, nor CD8(+) T-cells participated in the regulation. Further, **CD4**(+) T-cells of mice immunized with OVA-liposome were capable of inducing antigen-specific IgE synthesis in athymic nude mice immunized with alum-adsorbed OVA. On the other hand, immunization of the recipient mice with OVA-liposome did not induce anti-OVA IgE production, even when **CD4**(+) T-cells of mice immunized with alum-adsorbed OVA were transferred. In the secondary immune response, OVA-liposome enhanced anti-OVA IgG antibody production but not the ongoing IgE production, suggesting that the IgE-selective unresponsiveness induced by the liposomal antigen involved direct effects on IgE but not IgG switching in vivo. These results suggest the role of an alternative mechanism, one not involving T-cells, in the regulation of IgE synthesis, and raise the possibility that surface-linked liposomal antigen is potentially applicable for the development of a novel vaccine that induces the least IgE synthesis. Moreover, given the relatively low allergic response to and increased antigenicity of the allergen, this form of antigen preparation would be applicable to allergen immunotherapy.

L12 ANSWER 2 OF 7 MEDLINE on STN DUPLICATE 2
2002623666. PubMed ID: 12370355. T cell-independent regulation of IgE antibody production induced by surface-linked liposomal antigen. Taneichi Maiko; Naito Seishiro; Kato Hiroshi; Tanaka Yuriko; Mori Masahito; Nakano Yoshio; Yamamura Hiroyuki; Ishida Hiroshi; Komuro Katsutoshi; Uchida Tetsuya. (Department of Safety Research on Blood and Biological Products, National Institute of Infectious Diseases, 4-7-1 Gakuen, Musashimurayama-city, Tokyo 208-0011, Japan.) Journal of immunology (Baltimore, Md. : 1950), (2002 Oct 15) 169 (8) 4246-52. Journal code:

2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Control of IgE Ab production is important for the prevention of IgE-related diseases. However, in contrast to the existing information on the induction of IgE production, little is known about the regulation of the production of this isotype, with the exception of the well-documented mechanism involving T cell subsets and their cytokine products. In this study, we demonstrate an alternative approach to interfere with the production of IgE, independent of the activity of T cells, which was discovered during the course of an investigation intended to clarify the mechanism of IgE-selective unresponsiveness induced by surface-coupled liposomal Ags. Immunization of mice with OVA-**liposome conjugates** induced IgE-selective unresponsiveness without apparent Th1 polarization. Neither IL-12, IL-10, nor CD8(+) T cells participated in the regulation. Furthermore, **CD4**(+) T cells of mice immunized with OVA-liposome were capable of inducing Ag-specific IgE synthesis in athymic nude mice immunized with alum-adsorbed OVA. In contrast, immunization of the recipient mice with OVA-liposome did not induce anti-OVA IgE production, even when **CD4**(+) T cells of mice immunized with alum-adsorbed OVA were transferred. In the secondary immune response, OVA-liposome enhanced anti-OVA IgG Ab production, but it did not enhance ongoing IgE production, suggesting that the IgE-selective unresponsiveness induced by the liposomal Ag involved direct effects on IgE, but not IgG switching in vivo. These results suggest the existence of an alternative mechanism not involving T cells in the regulation of IgE synthesis.

L12 ANSWER 3 OF 7 MEDLINE on STN DUPLICATE 3

2002720816. PubMed ID: 12483036. Selective inhibition of systemic anti-OVA IgE production in response to oral pre-treatment with OVA-**liposome conjugates.** Naito Seishiro; Taneichi Maiko; Kato Hiroshi; Tanaka Yuriko; Ami Yasushi; Suzaki Yuriko; Mori Masahito; Nakano Yoshio; Yamamura Hiroyuki; Morokuma Kazunori; Ohkuma Kunio; Miyake Hidekazu; Kiniwa Mamoru; Komuro Katsutoshi; Uchida Tetsuya. (Department of Safety Research on Blood and Biological Products, National Institute of Infectious Diseases, Musashimurayama, Tokyo, Japan.) International archives of allergy and immunology, (2002 Dec) 129 (4) 314-9. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB BACKGROUND: We have previously reported that intraperitoneal injection with OVA-**liposome conjugates** induces OVA-specific and IgE-selective unresponsiveness in mice. METHODS: In the present study, the effects of oral pre-treatment with OVA-**liposome conjugates** or with plain OVA solution on anti-OVA IgG antibody production were investigated in mice after subsequent immunization with alum-adsorbed OVA. Control mice received only the immunization. RESULTS: The levels of serum anti-OVA IgG antibody in mice receiving oral administration of OVA-liposome were comparable to those in the control mice. However, in mice receiving oral administration of the same dose of plain OVA, levels of serum anti-OVA IgG antibody were significantly lower than those in control mice. Surprisingly, anti-OVA IgE antibody production was completely inhibited in mice receiving oral administration of OVA-**liposome conjugates.** Splenic **CD4**(+) T cells of mice receiving oral administration of OVA-liposome and those of control mice produced comparable levels of cytokines, while those of mice receiving oral administration of plain OVA solution produced significantly lower levels of cytokines than those in the other two groups. CONCLUSION: Orally administered OVA-liposome did not affect anti-OVA IgG production but did inhibit anti-OVA IgE antibody production, while orally administered OVA solution inhibited production of both IgG and IgE antibodies. These results suggest that antigen-**liposome conjugates** can possibly be orally administered in order to control antigen-specific IgE antibody production, without affecting IgG antibody production.

L12 ANSWER 4 OF 7 CAPLUS

1999:119837 Document No. 130:195756 **Conjugates** of polymers and antibodies specific for T lymphocytes, and their use as adjuvants. Chang, Tse Wen (Tanox Biosystems, Inc., USA). U.S. US 5872222 A 19990216, 6 pp., Cont.-in-part of U.S. Ser. No. 926.566, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1992-993291 19921218. PRIORITY: US 1991-688000 19910419; US 1992-819449 19920110; US 1992-926566 19920806.

AB Disclosed are **conjugates** including a substantially nonimmunogenic polymer backbone or microbead and binding mols., such as Fv, Fab, or F(ab')2 fragments of monoclonal antibodies or whole antibodies that are bound through their Fc carbohydrate moieties or have their Fc portion modified so that they cannot effect ADCC (antibody-dependent cellular cytotoxicity) or complement-mediated cytolysis, and that are specific for a T cell surface antigen, such as CD3, TCR, **CD4**, CD8, or CD28 on T cells. The polymer or microbead is preferably made of cross-linked dextran, ficoll, latex, or agarose, and is preferably of 0.1 to 10 μm in size, so that it can be suspended in fluids for in vivo applications. These **conjugates** can be used as adjuvants to enhance the antibody response against an administered immunogen.

L12 ANSWER 5 OF 7 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

1999:736069 The Genuine Article (R) Number: 225QX. Cytokine production by **CD4**(+) T cells of mice immunised with antigen-**liposome conjugates**.. Horino A (Reprint); Naito S; Taneichi M; Kato H; Komuro K; Uchida T. NATL INST INFECT DIS, TOKYO 2080011, JAPAN. JOURNAL OF LEUKOCYTE BIOLOGY (JUN 1999) Supp. [S], pp. 55-55. Publisher: FEDERATION AMER SOC EXP BIOL. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998. ISSN: 0741-5400. Pub. country: JAPAN. Language: English.

L12 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

1999:408928 Document No.: PREV199900408928. Cytokine production by **CD4** + T cells of mice immunized with antigen-**liposome conjugates.** Horino, A. [Reprint author]; Naito, S. [Reprint author]; Taneichi, M. [Reprint author]; Kato, H. [Reprint author]; Komuro, K. [Reprint author]; Uchida, T. [Reprint author]. National Institute of Infectious Diseases, Tokyo, 208-0011, Japan. Journal of Leukocyte Biology, (1999) No. SUPPL., pp. 18. print.
Meeting Info.: 15th International Congress of the Society for Leukocyte Biology with the European Macrophage Study Group. Cambridge, England, UK. September 22-26, 1999.
CODEN: JLBIE7. ISSN: 0741-5400. Language: English.

L12 ANSWER 7 OF 7 MEDLINE on STN DUPLICATE 4

90203581. PubMed ID: 1969450. Lymphocyte proliferative responses to soluble and liposome-conjugated envelope peptides of HIV-1. Krowka J; Stites D; Debs R; Larsen C; Fedor J; Brunette E; Duzgunes N. (Department of Laboratory Medicine, University of California, San Francisco 94143.) Journal of immunology (Baltimore, Md. : 1950), (1990 Apr 1) 144 (7) 2535-40. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB The proliferation of lymphocytes from HIV-seronegative (HIV Ab-) and seropositive (HIV Ab+) individuals in response to two synthetic peptide epitopes of HIV envelope glycoproteins (ENVgp) was evaluated as an index of cell-mediated immunity in infected individuals. All HIV Ab- and most HIV Ab+ individuals' lymphocytes failed to proliferate in primary cultures in response to the two soluble HIV ENVgp peptides, ENVP346 and ENVP466 even in the presence of rIL-2. After stimulation with **liposome-conjugates** of ENVP346 or ENVP466 and soluble rIL-2, however, **CD4** lymphocytes from some HIV Ab+ individuals were able to proliferate. Significantly higher frequencies of rIL-2-augmented proliferative responses to liposome-conjugated ENVP346 or ENVP466 were observed in HIV Ab+ asymptomatic individuals as compared to patients with AIDS-related conditions or AIDS. These studies indicate that the conjugation of HIV peptides or proteins to liposomes and stimulation with rIL-2 may enhance cell-mediated responses to these peptides.

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=> d his

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     FILE 'STNGUIDE' ENTERED AT 09:38:36 ON 09 AUG 2004

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 09:38:50 ON
     09 AUG 2004
L1             0 S LIPSOME CONJUGATE
L2           304 S LIPOSOME CONJUGATE
L3             0 S L2 AND ANTI-CD4
L4             1 S L2 AND HLA
L5           880 S HLA-DR ANTIBOD?
L6             0 S L5 AND CONJUGATED LIPOSOME
L7             8 S L5 AND CONJUGATE
L8             2 S L7 AND LIPOSOME
L9             2 DUP REMOVE L8 (0 DUPLICATES REMOVED)
L10          304 S L2 AND CONJUGATE
L11           18 S L10 AND CD4
L12            7 DUP REMOVE L11 (11 DUPLICATES REMOVED)

=> s l10 and anti-HLA-DR
L13            0 L10 AND ANTI-HLA-DR

=> s l10 and HLA
L14            1 L10 AND HLA

=> d l14 cbib abs

L14  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2004 ACS on STN
1999:119837   Document No. 130:195756  Conjugates of polymers and
     antibodies specific for T lymphocytes, and their use as adjuvants.  Chang,
     Tse Wen (Tanox Biosystems, Inc., USA).  U.S. US 5872222 A  19990216, 6
     pp., Cont.-in-part of U.S. Ser. No. 926.566, abandoned.  (English).
     CODEN: USXXAM.  APPLICATION: US 1992-993291 19921218.  PRIORITY: US
     1991-688000 19910419; US 1992-819449 19920110; US 1992-926566 19920806.
AB   Disclosed are conjugates including a substantially
     nonimmunogenic polymer backbone or microbead and binding mols., such as
     Fv, Fab, or F(ab')2 fragments of monoclonal antibodies or whole antibodies
     that are bound through their Fc carbohydrate moieties or have their Fc
     portion modified so that they cannot effect ADCC (antibody-dependent
     cellular cytotoxicity) or complement-mediated cytolysis, and that are
     specific for a T cell surface antigen, such as CD3, TCR, CD4, CD8, or CD28
     on T cells.  The polymer or microbead is preferably made of cross-linked
     dextran, ficoll, latex, or agarose, and is preferably of 0.1 to 10 μm
     in size, so that it can be suspended in fluids for in vivo applications.
     These conjugates can be used as adjuvants to enhance the
     antibody response against an administered immunogen.


=> s l10 and ATPase
L15            0 L10 AND ATPASE

=> dup remove l10
PROCESSING COMPLETED FOR L10
L16          179 DUP REMOVE L10 (125 DUPLICATES REMOVED)

=> s l16 and host membrane
L17            0 L16 AND HOST MEMBRANE

=> d l16 1-179 cbib abs

L16  ANSWER 1 OF 179  CAPLUS  COPYRIGHT 2004 ACS on STN
2004:41311   Document No. 140:133818  Conjugates of photosensitizers
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and oligonucleotides for selective photochemotherapy. Van Den Bergh, Hubert; Lange, Norbert (Ecole Polytechnique Federale De Lausanne, Switz.). PCT Int. Appl. WO 2004004769 A1 20040115, 82 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-EP8052 20030704. PRIORITY: GB 2002-15534 20020704.

AB This invention relates to oligonucleotide targeting agents and their use in the treatment of diseased cells by selective photochemotherapy (PCT). PCT is a method of treating human diseases and disorders, bacteriol. indications and other pathol. conditions. PCT is based on the topical or systemic application of a photosensitizing agent, a precursor or pro-drug thereof, which preferentially accumulates in the target tissue. Irradiation of the photosensitizing agent located in the target. tissue with electromagnetic radiation of an appropriate wavelength and the interaction of the thus excited photosensitive moiety with oxygen leads to tissue damage and destruction of the irradiated areas. As example of a therapeutic agent of the present invention, a single-stranded nucleic acid sequence complementary to a preselected target sequence (such as epidermal growth factor receptor mRNA) is conjugated to a photosensitizer (pheophorbide a, chlorin e6). The nucleic acid is also conjugated to a moiety that quenched excited energy of the photosensitizer. Such a moiety may be another photosensitizer, a fluorophore, a non-fluorescing dye or a gold nanoparticle. Inhibition of human colon cancer cells using the EGRF mRNA targeted agent is described.

L16 ANSWER 2 OF 179 MEDLINE on STN DUPLICATE 1

2004033918. PubMed ID: 14733581. Liposomes with differential lipid components exert differential adjuvanticity in antigen-**liposome conjugates** via differential recognition by macrophages. Tanaka Yuriko; Kasai Michiyuki; Taneichi Maiko; Naito Seishiro; Kato Hiroshi; Mori Masahito; Nishida Mitsuhiro; Maekawa Naoya; Yamamura Hiroyuki; Komuro Katsutoshi; Uchida Tetsuya. (Department of Safety Research on Blood and Biological Products, National Institute of Infectious Diseases, Tokyo 208-0011, Japan.) Bioconjugate chemistry, (2004 Jan-Feb) 15 (1) 35-40. Journal code: 9010319. ISSN: 1043-1802. Pub. country: United States. Language: English.

AB We previously reported that liposomes having differential lipid components displayed differential adjuvant effects when antigen was coupled with liposomes via glutaraldehyde. In the present study, antigen-**liposome conjugates** prepared using liposomes having differential lipid components were added to the macrophage culture, and phagocytosis and the antigen digest of liposome-coupled antigen by macrophages were then investigated. Antigen presentation by macrophages to an antigen-specific T-cell clone was further investigated using the same **conjugates.** Antigen-**liposome conjugates** which induced higher levels of antibody production in vivo were recognized more often, and the liposome-coupled antigen was digested to a greater degree by macrophages than antigen-**liposome conjugates** which induced lower levels of antibody production. These results correlated closely with those regarding antigen presentation by macrophages; when antigen was coupled to liposomes showing higher adjuvant effect, macrophages cocultured with antigen-**liposome conjugates** activated antigen-specific T-cells at a higher degree. The concentration of OVA in the macrophage culture added as antigen-**liposome conjugates** was approximately 32 microg/mL. However, the extent of T-cell activation was almost equal to that when 800 microg/mL of soluble OVA was added to the culture. The results of the present study demonstrated that the adjuvant activity of liposomes observed primary in vivo correlated closely with the recognition of

antigen-**liposome conjugates** and antigen presentation of liposome-coupled antigen by macrophages, suggesting that the adjuvant effects of liposomes are exerted at the beginning of the immune response, i.e., recognition of antigen by antigen-presenting cells.

L16 ANSWER 3 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2004:170325 Document No. 140:228789 Tumour cell targeting of stabilized **liposome conjugates**: experimental studies using boronated DNA-binding agents. Bohl Kullberg, Erika (Uppsala Universitet, Uppsala, Swed.). 72 pp. Avail. From degree-granting institution From: Diss. Abstr. Int., C 2003, 64(3), 668 (English) 2003.
AB Unavailable

L16 ANSWER 4 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2003:777622 Document No. 139:275730 Antibody fusion proteins: effective adjuvants of protein vaccination. Penichet, Manuel L.; Morrison, Sherie L.; Peng, Lisan; Dela Cruz, Jay (The Regents of the University of California, USA). PCT Int. Appl. WO 2003080106 A1 20031002, 90 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US9136 20030321. PRIORITY: US 2002-PV366917 20020321; US 2002-118473 20020405.
AB The authors disclose antibody-immunostimulant fusion proteins as adjuvants of antigenic protein vaccinations that elicit humoral and/or cellular immune responses in vaccinated subjects. In one example, humoral and cellular immune responses against HER2 where induced by an anti-HER2 IgG3 chimeric antibody expressing the variable domains of Herceptin.

L16 ANSWER 5 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2003:242474 Document No. 138:270287 Mutated peptides of HIV reverse transcriptase and their use for vaccination and diagnostic purposes. Autran, Brigitte; Samr, I. Assia; Debre, Patrice; Calvez, Vincent; Katlama, Christine; Haas, Gaby (Universite Pierre et Marie Curie - Paris VI, Fr.). PCT Int. Appl. WO 2003025166 A1 20030327, 57 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (French). CODEN: PIXXD2. APPLICATION: WO 2001-FR2872 20010914.
AB The invention concerns treatment of infectious pathologies comprising a anti-infective chemotherapeutic treatment phase inducing resistance mutations and a therapeutic vaccination phase directed against said resistance mutations and the agents used in said treatment. More particularly, the invention concerns peptides of 8-80 amino acids of the HIV reverse transcriptase sequence and comprising at least a mutation with respect to said wild-type sequence of said enzyme, the mutation induced in response to treatments by nucleoside and non-nucleoside reverse transcriptase inhibitors. The invention also concerns a pharmaceutical composition or vaccine based on said peptides, for inducing an immune response specific to said mutated sequences and for enhancing or prolonging the efficiency of treatments with nucleoside or non-nucleoside reverse transcriptase inhibitors. The invention further concerns epitopes derived from said peptide sequences to evaluate the specific immune response following the vaccine injection.

L16 ANSWER 6 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2003:133121 Document No. 138:183234 **Conjugates** of macrocyclic metal complexes with biomolecules, and the use thereof for producing agents for use in NMR diagnosis, radiodiagnosis and radiotherapy. Platzek, Johannes; Schmitt-Willich, Heribert; Michl, Guenther; Frenzel, Thomas; Suelzle, Detlev; Bauer, Hans; Raduechel, Bernd; Weinmann, Hanns-Joachim; Schirmer, Heiko (Schering AG, Germany). PCT Int. Appl. WO 2003013617 A2 20030220, 93 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2. APPLICATION: WO 2002-EP8000 20020718. PRIORITY: DE 2001-10135355 20010720.

AB The invention discloses **conjugates** of macrocyclic metal complexes with biomols., as well as the production thereof. The **conjugates** are suited for use as contrast agents in NMR diagnosis and radiodiagnosis and as agents for radiotherapy. A high relaxivity is achieved and a fine tuning of the relaxivity is made possible by a special liganding of the macrocycles.

L16 ANSWER 7 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2003:757312 Document No. 139:296917 **Conjugates** of membrane translocating peptides and pharmaceutically active agents. O'Mahony, Daniel; Lambkin, Imelda; Pinilla, Clemencia; Houghten, Richard (Ire.). U.S. Pat. Appl. Publ. US 2003181367 A1 20030925, 31 pp., Cont.-in-part of U.S. Ser. No. 671,089. (English). CODEN: USXXCO. APPLICATION: US 2002-126845 20020419. PRIORITY: US 1999-PV156246 19990927; US 2000-671089 20000927.

AB The present invention provides membrane translocating peptides (hereinafter referred to interchangeably either as "MTLPs" or "translocating peptides") or nucleotide sequences coding therefore, MTLP-active agent complexes and MTLP-active particle complexes, wherein the MTLP enhances movement of the active agent or the active particle across a lipid membrane. More particularly, the present invention provides a MTLP, MTLP-active agent complexes and MLTP-active particle complexes, wherein the MTLP enhances movement of the active agent or of the active particle into a cell, into and out of an intracellular compartment and across a cell layer in an animal, including a human. Methods of making and methods of using MTLPs, MTLP-active agent complexes and MTLP-active particle complexes also are included.

L16 ANSWER 8 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2003:449827 Document No. 139:35095 Human interleukin 13 (IL13) mutants with varying specificity for the IL13 receptors, IL13/cytotoxin **conjugates** and therapeutic uses. Debinski, Waldemar; Thompson, Jeffrey P. (The Penn State Research Foundation, USA). U.S. US 6576232 B1 20030610, 36 pp., Cont.-in-part of U.S. Ser. No. 54,711. (English). CODEN: USXXAM. APPLICATION: US 2000-679710 20001005. PRIORITY: US 1998-54711 19980403; US 1999-PV157934 19991006.

AB This invention provides mutant human interleukin 13 mols. showing varying specificity for the restricted (IL4 independent) IL13 receptor. The mutant hIL13 mols. include those made by substituting the amino acid residues that occur in the alpha-helix regions of native hIL13 with various other amino acid residues. Some of the mutants retain the ability to bind and cause signaling through IL13 receptors, while other mutants do not. These mutants may be useful for therapy of interleukin 13-related diseases. Multiply mutated forms of hIL13 conjugated to cytotoxins are used to preferentially target diseased cells over non-diseased cells. Radioimmunodetection and radio-immunotherapy of human high grade glioma cells was demonstrated.

L16 ANSWER 9 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2003:521340 Document No. 139:250122 Synthesis of an amphiphilic tetraantennary mannosyl **conjugate** and incorporation into liposome carriers. Espuelas, Socorro; Haller, Philippe; Schuber, Francis; Frisch, Benoit (Faculte de Pharmacie, Laboratoire de Chimie Bioorganique, Universite Louis Pasteur, UMR 7514 CNRS/ULP, Illkirch, 67400, Fr.). Bioorganic & Medicinal Chemistry Letters, 13(15), 2557-2560 (English) 2003. CODEN: BMCLE8. ISSN: 0960-894X. Publisher: Elsevier Science B.V..

AB We have synthesized a novel **conjugate** (Man4K3DOG) composed of a tetramannosyl head group connected, via a polyethylene glycol spacer, to a lipid moiety. This amphiphilic mol. was easily incorporated into the bilayers of liposomes. As expected from the clustering effect, such multivalent mannose residues when exposed on the surface of the vesicles showed much higher binding affinity for Con A than their monomannosyl analog. Mannosylated liposomes prepared with the tetravalent antenna could be promising carriers for e.g., loading dendritic cells with antigens for vaccination purposes.

L16 ANSWER 10 OF 179 MEDLINE on STN DUPLICATE 2
2003509066. PubMed ID: 14586483. STX-**liposome conjugates** as candidate vaccines. Uchida Tetsuya. (Department of Safety Research on Blood and Biological Products, National Institute of Infectious Diseases, Tokyo, Japan.. tuchida@nih.go.jp) . Drugs of today (Barcelona, Spain : 1998), (2003 Sep) 39 (9) 673-93. Ref: 68. Journal code: 101160518. ISSN: 0025-7656. Pub. country: Spain. Language: English.

AB Infection with Shiga toxin-producing (Stx) Escherichia coli (STEC) currently represents a serious public health problem due to its life-threatening complications: hemorrhagic colitis and hemolytic uremic syndrome. An inability to induce neutralizing antibody in response to primary STEC infection has been reported in STEC-infected humans. Therefore, active immunization with detoxified Stx to induce the production of neutralizing antibodies against Stx is currently an attractive option. Although this would not prevent the spread of infection, it would protect against death caused by cytotoxin-producing E. coli infection. Stx coupled with liposomes effectively induced protection against challenge with lethal doses of Stx in mice and in monkeys. Unique characteristics of antigen-**liposome conjugates** found in our investigations are reviewed, and the possible application of Stx-**liposome conjugates** in vaccines for the prevention of life-threatening systemic complications caused by STEC infection is discussed.

L16 ANSWER 11 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2003:443384 Document No. 140:138814 Improvement of transduction efficiency of recombinant adenovirus vector conjugated with cationic liposome for human oral squamous cell carcinoma cell lines. Fukuhara, Hirokazu; Hayashi, Yasushi; Yamamoto, Noriyuki; Fukui, Takafumi; Nishikawa, Masaya; Mitsudo, Kenji; Tohnai, Iwai; Ueda, Minoru; Mizuno, Masaaki; Yoshida, Jun (Department of Oral and Maxillofacial Surgery, Nagoya University Graduate School of Medicine, Showa-ku, Nagoya, 466-8550, Japan). Oral Oncology, 39(6), 601-609 (English) 2003. CODEN: EJCCER. ISSN: 1368-8375. Publisher: Elsevier Science Ltd..

AB Adenovirus (Ad) vectors are commonly used in gene therapy trials because of their efficiency in gene transfer. However, their use is limited by immune responses that reduce transgene expression and decrease the efficiency of repeated vector administration. In this study, the efficacy of gene transduction and the tumor-cell killing effect on four human oral (SAS, HSC-2, HSC-3, HSC-4) and one murine squamous cell carcinoma cell lines in vitro with Ad vector conjugated with cationic liposome (Ad/SUV) was evaluated. Ad/SUV resulted in two to five-fold over higher transduction efficiency in four human and one murine cell lines in vitro than Ad vector alone. The optimal Ad-SUV ratio was determined as 106 pfu of Ad vector with 1 μmol SUV. Ad/SUV showed more tumor-cell killing effect than Ad vector alone. Furthermore, the shielding effects of Ad vector

with Ad/SUV from neutralizing antibody were evaluated. We also found that Ad/SUV is less susceptible to inactivation by neutralizing antibodies in vitro. The efficacy of gene transduction with Ad vector was blocked more than 70% with neutralizing serum, while Ad/SUV retained approx. 50% of the control activity in vitro. On the basis of these results, the antitumor effect with suicide gene therapy using Ad/SUV in vivo was evaluated. Three injections of Ad/SUV showed the inhibition of tumor growth compared with control in vivo. Our results suggested that an enhanced antitumor effect on human oral squamous cell carcinoma would be obtained with repeated administrations of Ad/SUV.

L16 ANSWER 12 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2003:637400 Polymeric recognition of bacterial spores. Levon, Kalle M.; Ji, Tao; Kaholek, Marian; Kazakov, Sergey; Tarasenko, Olga M.; Sharma, Nawal K.; Yu, Bin; Zhou, Yanxiu (Department of Chemical Engineering, Chemistry, and Materials Science, Polymer Research Institute, Polytechnic University, Brooklyn, NY, 11201, USA). Abstracts of Papers, 226th ACS National Meeting, New York, NY, United States, September 7-11, 2003, POLY-520. American Chemical Society: Washington, D. C. (English) 2003. CODEN: 69EKY9.
AB Ligand-polymer **conjugates** were synthesized and evaluated for optimal binding to bacterial spores. Similarly, ligand-**liposome conjugates** were screened for biomarker applications. Eventually, the binding of bacteria was investigated on surfaces using modified ITO electrodes and the changes in ion activities were followed using potentiometry.

L16 ANSWER 13 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2003:627577 Document No. 140:258806 Introductory experiments on ligand liposomes as delivery agents for boron neutron capture therapy. Kullberg, Erika Bohl; Carlsson, Joergen; Edwards, Katarina; Capala, Jacek; Sjoeberg, Stefan; Gedda, Lars (Division of Biomedical Radiation Sciences, Rudbeck Laboratory, Uppsala University, Uppsala, 75185, Swed.). International Journal of Oncology, 23(2), 461-467 (English) 2003. CODEN: IJONES. ISSN: 1019-6439. Publisher: International Journal of Oncology.
AB Liposomes are, when coupled to receptor ligands, candidates for receptor mediated delivery of boron for tumor therapy since they have capacity to deliver large amts. of boron per receptor interaction. With EGF-liposomes the authors present a pegylated ligand liposome delivery vehicle, containing water soluble boronated phenanthridine, WSP1, or water soluble boronated acridine, WSA1, for EGFR targeting. In the case of WSA1 a ligand dependent uptake was obtained and the boron uptake was as good as if free WSA1 was given. No ligand dependent boron uptake was seen for WSP1 containing liposomes. Thus, WSA1 is a candidate for further studies. Approx. 105 boron atoms were in each liposome. A critical assessment indicates that after optimization up to 106 boron atoms can be loaded. Since it is known that, for therapeutic effect, approx. 108-109 boron atoms are needed in a single tumor cell it is realized that 102-103 receptor interactions are needed to meet the demand. Tests applying cultured glioma cells indicate, without optimization of the delivery conditions, a boron uptake in the ppm range, which is necessary for successful BNCT. Thus, it seems possible to kill micro-invasive tumor cells with targeted liposomes if the delivery conditions are optimal.

L16 ANSWER 14 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2003:1013941 Document No. 140:246373 Anti-neovascular therapy by liposomal drug targeted to membrane type-1 matrix metalloproteinase. Kondo, Masami; Asai, Tomohiro; Katanasaka, Yasufumi; Sadzuka, Yasuyuki; Tsukada, Hideo; Ogino, Koichi; Taki, Takao; Baba, Kazuhiko; Oku, Naoto (Department of Medical Biochemistry and COE Program in the 21st Century, University of Shizuoka School of Pharmaceutical Sciences, Shizuoka, Japan). International Journal of Cancer, Volume Date 2004, 108(2), 301-306 (English) 2003. CODEN: IJCNAW. ISSN: 0020-7136. Publisher: Wiley-Liss, Inc..
AB Because membrane type-1 matrix metalloproteinase (MTI-MMP) is expressed

specifically on the angiogenic endothelium as well as tumor cells, an agent possessing the ability to bind to this mol. might be useful as a tool for active targeting of tumor angiogenic vessels. Based on the sequences of peptide substrates of MTI-MMP, which had been determined by a phage-displayed peptide library, the authors examined the binding ability of peptide-modified liposomes for endothelial cells and targeting ability for tumor tissues by positron emission tomog. (PET). Liposomes modified with stearoyl-Gly-Pro-Leu-Pro-Leu-Arg (GPLPLR-Lip) showed high binding ability to human umbilical vein endothelial cells and accumulated in the tumor about 4-fold more than did the unmodified liposomes. Because the authors reported previously that liposomalized 5'-O-dipalmitoylphosphatidyl 2'-C-cyano-2'-deoxy-1-β-D-arabino-pentofuranosylcytosine (DPP-CNDAC), a hydrophobized derivative of the novel antitumor nucleoside CNDAC, strongly suppressed tumor growth when delivered in liposomes modified with another angiogenic homing peptide, the authors examined the antitumor activity of DPP-CNDAC entrapped in GPLPLR-Lip. DPP-CNDAC/GPLPLR-Lip showed significant tumor growth suppression compared to DPP-CNDAC/unmodified liposomes. These results suggest that DPP-CNDAC-liposomes modified with MTI-MMP-targeted peptide are useful for cancer anti-neovascular therapy (ANET), namely, tumor growth suppression by damage to angiogenic endothelial cells.

L16 ANSWER 15 OF 179 MEDLINE on STN DUPLICATE 3

2003122138. PubMed ID: 12636161. Tumor-cell targeted epiderimal growth factor liposomes loaded with boronated acridine: uptake and processing. Kullberg Erika Bohl; Nestor Marika; Gedda Lars. (Division of Biomedical Radiation Sciences, Department of Oncology, Radiology and Clinical Immunology, Rudbeck Laboratory, Uppsala University, S-751 85 Uppsala, Sweden.. Erika.Bohl@bms.uu.se) . Pharmaceutical research, (2003 Feb) 20 (2) 229-36. Journal code: 8406521. ISSN: 0724-8741. Pub. country: United States. Language: English.

AB PURPOSE: The aim of this work was to investigate the cellular binding and processing of polyethylene glycol-stabilized epidermal growth factor (EGF) liposomes. The liposomes were actively loaded with water-soluble boronated acridine (WSA), primarily developed for boron neutron capture therapy. METHODS: The uptake, internalization, and retention of EGF-**liposome conjugates** were studied in two cultured monolayer cell-lines, A-431 and U-343, with regard to the nuclide-label on the targeting agent, the carrier, and the load. The subcellular localization of WSA was studied using confocal microscopy. RESULTS: We found that the liposome complex was internalized after specific binding to the EGF receptor. After internalization in the tumor cells, WSA was distributed mainly in the cytoplasm and was shown to have long cellular retention, with 80% of the boron remaining after 48 h. CONCLUSIONS: The long retention of the compound and the cellular boron concentration reached makes these targeted liposomes interesting for further development toward boron neutron capture therapy.

L16 ANSWER 16 OF 179 MEDLINE on STN DUPLICATE 4

2003405493. PubMed ID: 12944143. New cationized LDL-DNA complexes: their targeted delivery to fibroblasts in culture. Khan Zainub; Hawtrey Arthur O; Ariatti Mario. (Biochemistry, School of Life and Environmental Sciences, University of Durban-Westville, Durban, South Africa.) Drug delivery, (2003 Jul-Sep) 10 (3) 213-20. Journal code: 9417471. ISSN: 1071-7544. Pub. country: England: United Kingdom. Language: English.

AB Low density lipoproteins (LDL) have been cationized using the water-soluble carbodiimide, N-ethyl-N'-(3-trimethylpropylammonium) carbodiimide iodide at a reagent: lipoprotein mole ratio of 10 000:1. This was shown to increase the innate DNA-binding capacity of LDL 10-fold. [125I]-labeled carbodiimide-modified LDL ([125I])-labeled ECDI-LDL) appeared to recognize the LDL receptor on normal human skin fibroblasts, although some nonspecific binding also was detected. To demonstrate the large ionic component in the lipoprotein-DNA interactions, varepsilon -NH2 amino groups on the apolipoprotein B-100 (apoB-100) component of LDL were acetylated with acetic anhydride. A nitrocellulose filter-binding assay

revealed that acetylated LDL bound approximately 25% of the [3H]-labeled pBR322 plasmid DNA bound by native LDL under the same conditions. ECDI-LDL-[3H]-labeled plasmid DNA complexes were considerably more stable to NaCl challenge than complexes formed between [3H]-labeled plasmid DNA and native LDL. Thus, the half dissociation of ECDI-LDL containing complexes was achieved at 0.28 M NaCl, whereas for LDL-plasmid DNA complexes this was reached at 0.18 M NaCl. Displacement studies with native LDL studies showed that ECDI-LDL-[3H]-labeled plasmid DNA complexes retained the ability to recognize the LDL receptor on normal skin fibroblasts. Finally, ECDI-LDL complexes with pSV2CAT expression plasmid were shown to transfect CV-1 fibroblasts, a cell line known to specifically recognize apoB-**liposome conjugates.**

L16 ANSWER 17 OF 179 MEDLINE on STN DUPLICATE 5
2003247355. PubMed ID: 12769784. Surface-linked liposomal antigen induces IgE selective unresponsiveness in a T-cell independent fashion. Uchida Tetsuya. (Department of Safety Research on Blood and Biological Products, National Institute of Infectious Diseases, Musashimurayama-city, Tokyo, Japan.. tuchida@nih.go.jp) . Current drug targets. Immune, endocrine and metabolic disorders, (2003 Jun) 3 (2) 119-35. Ref: 58. Journal code: 101121150. ISSN: 1568-0088. Pub. country: Netherlands. Language: English.

AB We previously reported that surface-linked liposomal antigen induced IgE-selective unresponsiveness. The results were consistent even when different coupling procedures for antigen with liposomes, or for liposomes with different lipid components, were employed. During the course of an investigation intended to clarify the mechanism of IgE-selective unresponsiveness induced by surface-coupled liposomal antigens, we discovered an alternative approach to regulate the production of IgE, one that is independent of the activity of T-cells. Immunization of mice with OVA-**liposome conjugates** induced IgE- selective unresponsiveness without apparent Th1 polarization. Neither interleukin-12 (IL-12), IL-10, nor CD8(+) T-cells participated in the regulation. Further, CD4(+) T-cells of mice immunized with OVA-liposome were capable of inducing antigen-specific IgE synthesis in athymic nude mice immunized with alum-adsorbed OVA. On the other hand, immunization of the recipient mice with OVA-liposome did not induce anti-OVA IgE production, even when CD4(+) T-cells of mice immunized with alum-adsorbed OVA were transferred. In the secondary immune response, OVA-liposome enhanced anti-OVA IgG antibody production but not the ongoing IgE production, suggesting that the IgE-selective unresponsiveness induced by the liposomal antigen involved direct effects on IgE but not IgG switching in vivo. These results suggest the role of an alternative mechanism, one not involving T-cells, in the regulation of IgE synthesis, and raise the possibility that surface-linked liposomal antigen is potentially applicable for the development of a novel vaccine that induces the least IgE synthesis. Moreover, given the relatively low allergic response to and increased antigenicity of the allergen, this form of antigen preparation would be applicable to allergen immunotherapy.

L16 ANSWER 18 OF 179 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
2003:546047 Document No.: PREV200300548231. Polymeric recognition of bacterial spores. Levon, Kalle M. [Reprint Author]; Ji, Tao [Reprint Author]; Kaholek, Marian [Reprint Author]; Kazakov, Sergey [Reprint Author]; Tarasenko, Olga M. [Reprint Author]; Sharma, Nawal K. [Reprint Author]; Yu, Bin; Zhou, Yanxiu. Department of Chemical Engineering, Chemistry, and Materials Science, Polymer Research Institute, Polytechnic University, 6 MetroTech Center, Brooklyn, NY, 11201, USA. klevon@poly.edu. Abstracts of Papers American Chemical Society, (2003) Vol. 226, No. 1-2, pp. POLY 520. print.
Meeting Info.: 226th ACS (American Chemical Society) National Meeting. New York, NY, USA. September 07-11, 2003. American Chemical Society.
ISSN: 0065-7727 (ISSN print). Language: English.

L16 ANSWER 19 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2002:185276 Document No. 136:242898 Screening of peptide libraries to

identify highly specific ligands and cognate receptors for cell or tissue-specific targeting. Arap, Wadih; Pasqualini, Renata (Board of Regents, the University of Texas System, USA). PCT Int. Appl. WO 2002020722 A2 20020314, 298 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US27702 20010907. PRIORITY: US 2000-PV231266 20000908; US 2001-765101 20010117.

AB Methods of identify cell or tissue-specific peptide ligands and their cognate receptors for use in targeted drug delivery or gene therapy. A large number of targeting peptides directed towards human organs, tissues or cell types are disclosed. The peptides are of use for targeted delivery of therapeutic agents, including but not limited to gene therapy vectors. A novel class of gene therapy vectors is disclosed. Certain of the disclosed peptides have therapeutic use for inhibiting angiogenesis, inhibiting tumor growth, inducing apoptosis, inhibiting pregnancy or inducing weight loss. Methods of identifying novel targeting peptides in humans, as well as identifying endogenous receptor-ligand pairs are disclosed. Methods of identifying novel infectious agents that are causal for human disease states are also disclosed. A novel mechanism for inducing apoptosis is further disclosed. Screening of a phage display library by direct incubation with bone marrow to identify bone marrow-specific ligand peptides is demonstrated. The use of circulating antibodies from prostate cancer patients to identify the antigens. One of the antigens, identified as GRP78, was a strong indicator of survival time and could be used as a prognostic marker. Successful targeting of adeno-associated virus-based vectors to vascular endothelium is demonstrated.

L16 ANSWER 20 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

2002:185179 Document No. 136:215405 A single-chain antibody to human endoglin for use in the prevention of tumor vascularization. Kontermann, Roland; Miller, Daniel; Mueller, Rolf (Vectron Therapeutics A.-G., Germany). PCT Int. Appl. WO 2002020614 A2 20020314, 37 pp. DESIGNATED STATES: W: CA, JP, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (German). CODEN: PIXXD2. APPLICATION: WO 2001-EP10197 20010904. PRIORITY: DE 2000-10043481 20000904.

AB A single-chain antibody that specifically binds to the extracellular domain of the human endoglin (CD105 antigen) is described for use in the prevention of angiogenesis of tumors. The antibody was identified by screening a phage display library. A fusion protein of the antibody with an antibody to the knob protein of adenovirus 5 is prepared for use in the targeting of adenoviral gene therapy vectors to endothelial cells. Other uses for the antibody, including the use of fusion proteins with anti-CD3 antibodies to induce lysis of endothelial cells.

L16 ANSWER 21 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

2002:184891 Document No. 136:226786 Methods for inhibiting inflammatory disease with methyl benzoate compounds. Tuse, Daniel; Hiebert, Charles; Laderoute, Keith R.; Waleh, Nahid (Large Scale Biology Corporation, USA; SRI International). PCT Int. Appl. WO 2002020004 A1 20020314, 55 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US28155 20010906. PRIORITY: US 2000-656144 20000906.

AB The present invention relates to methods for effectively inhibiting

inflammatory diseases, such as Crohn's disease and ulcerative colitis. In other aspects, this invention relates to methods of reducing or inhibiting granulomas and inhibiting angiogenesis. Methyl-3,5-diiodo-4-(4'-methoxyphenoxy)benzoate was prepared and tested.

L16 ANSWER 22 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2002:658578 Document No. 137:200278 Human interleukin 13 substitution mutants and **conjugates** for diagnosis and treatment of cancer. Debinski, Waldemar (USA). U.S. Pat. Appl. Publ. US 2002119120 A1 20020829, 27 pp., Cont.-in-part of U.S. Ser. No. 54,711. (English). CODEN: USXXCO. APPLICATION: US 2001-938936 20010824. PRIORITY: US 1998-54711 19980403; US 2000-PV229194 20000830.
AB This invention provides mutant hIL13 mols. include those made by substituting one or more of the amino acid residues that occur in the alpha-helix regions of native hIL13 with various other amino acid residues. Multiply mutated forms of hIL13 conjugated to cytotoxins are used to preferentially target diseased cells over non-diseased cells.

L16 ANSWER 23 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2002:592290 Document No. 137:152012 Liposome analysis method. Mizuochi, Tsugio; Nakata, Munehiro; Yasuda, Atsushi (Tokai University, Japan; Nippon Zeon Co., Ltd.). Jpn. Kokai Tokkyo Koho JP 2002221515 A2 20020809, 7 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 2001-17893 20010126.
AB An anal. method is provided for rapidly measuring liposome components with high sensitivity and high accuracy using a high-performance liquid chromatog. apparatus

L16 ANSWER 24 OF 179 MEDLINE on STN DUPLICATE 6
2002623666. PubMed ID: 12370355. T cell-independent regulation of IgE antibody production induced by surface-linked liposomal antigen. Taneichi Maiko; Naito Seishiro; Kato Hiroshi; Tanaka Yuriko; Mori Masahito; Nakano Yoshio; Yamamura Hiroyuki; Ishida Hiroshi; Komuro Katsutoshi; Uchida Tetsuya. (Department of Safety Research on Blood and Biological Products, National Institute of Infectious Diseases, 4-7-1 Gakuen, Musashimurayama-city, Tokyo 208-0011, Japan.) Journal of immunology (Baltimore, Md. : 1950), (2002 Oct 15) 169 (8) 4246-52. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.
AB Control of IgE Ab production is important for the prevention of IgE-related diseases. However, in contrast to the existing information on the induction of IgE production, little is known about the regulation of the production of this isotype, with the exception of the well-documented mechanism involving T cell subsets and their cytokine products. In this study, we demonstrate an alternative approach to interfere with the production of IgE, independent of the activity of T cells, which was discovered during the course of an investigation intended to clarify the mechanism of IgE-selective unresponsiveness induced by surface-coupled liposomal Ags. Immunization of mice with OVA-**liposome conjugates** induced IgE-selective unresponsiveness without apparent Th1 polarization. Neither IL-12, IL-10, nor CD8(+) T cells participated in the regulation. Furthermore, CD4(+) T cells of mice immunized with OVA-liposome were capable of inducing Ag-specific IgE synthesis in athymic nude mice immunized with alum-adsorbed OVA. In contrast, immunization of the recipient mice with OVA-liposome did not induce anti-OVA IgE production, even when CD4(+) T cells of mice immunized with alum-adsorbed OVA were transferred. In the secondary immune response, OVA-liposome enhanced anti-OVA IgG Ab production, but it did not enhance ongoing IgE production, suggesting that the IgE-selective unresponsiveness induced by the liposomal Ag involved direct effects on IgE, but not IgG switching in vivo. These results suggest the existence of an alternative mechanism not involving T cells in the regulation of IgE synthesis.

L16 ANSWER 25 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2002:161704 Document No. 136:339680 A Strip Liposome Immunoassay for Aflatoxin B1. Ho, J. A. A.; Wauchope, R. D. (University of Georgia Coastal Plain Experiment Station, Tifton, GA, 31793, USA). Analytical

Chemistry, 74(7), 1493-1496 (English) 2002. CODEN: ANCHAM. ISSN: 0003-2700. Publisher: American Chemical Society.

AB A technique has been developed for the preparation of aflatoxin B1 (AFB1)-tagged liposomes encapsulating a visible dye. These liposomes have several useful potential anal. applications, one of which is demonstrated. A simple plastic-backed nitrocellulose strip is the basis for an assay for detecting AFB1. Samples containing aflatoxin B1 are allowed to migrate by capillary action along the strip into a zone containing immobilized antibodies; then aflatoxin B1-tagged, dye-containing liposomes are allowed to migrate into the same area, filling any remaining antibody sites. The liposomes that bound to the antibody zone exhibit an intense purplish pink color whose optical d. is inversely proportional to the aflatoxin concentration in the sample. The device is capable of detecting aflatoxin B1 at levels down to 20 ng and could serve as a rapid procedure for visual screening of agricultural and food samples for AFB1 or, with densitometry, as an inexpensive quant. assay.

L16 ANSWER 26 OF 179 MEDLINE on STN DUPLICATE 7

2002376057. PubMed ID: 12121129. Cholesterol inclusion in liposomes affects induction of antigen-specific IgG and IgE antibody production in mice by a surface-linked liposomal antigen. Nakano Yoshio; Mori Masahito; Yamamura Hiroyuki; Naito Seishiro; Kato Hiroshi; Taneichi Maiko; Tanaka Yuriko; Komuro Katsutoshi; Uchida Tetsuya. (DDS Development Division, NOF Corporation, Tokyo, Japan.) Bioconjugate chemistry, (2002 Jul-Aug) 13 (4) 744-9. Journal code: 9010319. ISSN: 1043-1802. Pub. country: United States. Language: English.

AB In the previous study, we investigated the induction of ovalbumin (OVA)-specific antibody production in mice by OVA-**liposome conjugates** made using four different lipid components, including unsaturated carrier lipid and three different saturated carrier lipids. All of the OVA-**liposome conjugates** tested induced IgE-selective unresponsiveness. The highest titer of anti-OVA IgG was observed in mice immunized with OVA-liposomes made using liposomes with the highest membrane fluidity, suggesting that the membrane fluidity of liposomes affects their adjuvant effect. In this study, liposomes with five different cholesterol inclusions, ranging from 0% to 43% of the total lipid, were made, and the induction of OVA-specific antibody production by OVA-**liposome conjugates** was compared among these liposome preparations. In contrast to the results in the previous study, liposomes that contained no cholesterol and possessed the lowest membrane fluidity demonstrated the highest adjuvant effect for the induction of IgG antibody production. In addition, when the liposomes with four different lipid compositions were used, OVA-**liposome conjugates** made using liposomes that did not contain cholesterol induced significantly higher levels of anti-OVA IgG antibody production than did those made using liposomes that contained cholesterol and, further, induced significant production of anti-OVA IgE. These results suggest that cholesterol inclusion in liposomes affects both adjuvanticity for IgG production and regulatory effects on IgE synthesis by the surface-coupled antigen of liposomes.

L16 ANSWER 27 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

2003:611430 Document No. 140:213048 Boron neutron-capture therapy (BNCT) by BSH-entrapped transferrin-PEG- liposome. Maruyama, K.; Kasaoka, S.; Yanagie, H.; Sakurai, Y.; Kobayashi, H.; Shinohara, A.; Chiba, M.; Ono, K. (Dept. of Biopharmaceutics, Teikyo Univ., Kanagawa, Japan). Research and Development in Neutron Capture Therapy, Proceedings of the International Congress on Neutron Capture Therapy, 10th, Essen, Germany, Sept. 8-13, 2002, 727-731. Editor(s): Sauerwein, Wolfgang; Moss, Raymond; Wittig, Andrea. Monduzzi Editore: Bologna, Italy. ISBN: 88-323-2909-3 (English) 2002. CODEN: 69EHTT.

AB TF-PEG liposomes encapsulating BSH showed a prolonged residence time in the circulation and low uptake by the reticuloendothelial system (RES) in Colon 26 tumor-bearing mice after iv injection, resulting in enhanced accumulation of 10B into the solid tumor tissue. Furthermore, TF-PEG

liposomes were internalized into tumor cells by receptor-mediated endocytosis after binding, causing tumor growth suppression in vivo upon thermal neutron irradiation TF-PEG liposomes have potential for as a new intracellular targeting carrier in BNCT therapy for cancer.

L16 ANSWER 28 OF 179 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
2002389921 EMBASE Folate-mediated delivery of macromolecular anticancer therapeutic agents. Lu Y.; Low P.S.. P.S. Low, Department of Chemistry, 1393 Brown Building, Purdue University, West Lafayette, IN 47907, United States. plow@purdue.edu. Advanced Drug Delivery Reviews 54/5 (675-693) 13 Sep 2002.
Refs: 93.
ISSN: 0169-409X. CODEN: ADDREP.
Publisher Ident.: S 0169-409X(02)00042-X. Pub. Country: Netherlands.
Language: English. Summary Language: English.
AB The receptor for folic acid constitutes a useful target for tumor-specific drug delivery, primarily because: (1) it is upregulated in many human cancers, including malignancies of the ovary, brain, kidney, breast, myeloid cells and lung, (2) access to the folate receptor in those normal tissues that express it can be severely limited due to its location on the apical (externally-facing) membrane of polarized epithelia, and (3) folate receptor density appears to increase as the stage/grade of the cancer worsens. Thus, cancers that are most difficult to treat by classical methods may be most easily targeted with folate-linked therapeutics. To exploit these peculiarities of folate receptor expression, folic acid has been linked to both low molecular weight drugs and macromolecular complexes as a means of targeting the attached molecules to malignant cells. Conjugation of folic acid to macromolecules has been shown to enhance their delivery to folate receptor-expressing cancer cells in vitro in almost all situations tested. Folate-mediated macromolecular targeting in vivo has, however, yielded only mixed results, largely because of problems with macromolecule penetration of solid tumors. Nevertheless, prominent examples do exist where folate targeting has significantly improved the outcome of a macromolecule-based therapy, leading to complete cures of established tumors in many cases. This review presents a brief mechanistic background of folate-targeted macromolecular therapeutics and then summarizes the successes and failures observed with each major application of the technology. .COPYRGT. 2002 Elsevier Science B.V. All rights reserved.

L16 ANSWER 29 OF 179 MEDLINE on STN DUPLICATE 8
2002292341. PubMed ID: 12031885. Radioiodination of glycoprotein-conjugated liposomes by using the Bolton-Hunter reagent and biodistribution in tumor-bearing mice. Shimura N; Sogawa Y; Kawakita Y; Ikekita M; Yamazaki N; Kojima S. (Faculty of Pharmaceutical Sciences, Science University of Tokyo, Tokyo, Japan.) Nuclear medicine and biology, (2002 May) 29 (4) 491-6. Journal code: 9304420. ISSN: 0969-8051. Pub. country: England: United Kingdom. Language: English.
AB We have developed a suitable radiolabeling method for our new type of glycoprotein-**liposome conjugate** (GCL), in order to investigate its potential utility as a drug carrier that can target the cellular functions of carbohydrate-binding proteins. In order to obtain radiolabeled GCL with high labeling efficiency, we introduced p-hydroxyphenylpropyl groups into the liposome membrane through the amine moiety of a constitutive phospholipid, dipalmitoylphosphatidylethanolamine (DPPE) by using Bolton-Hunter reagent (BHR). Radioiodination of the introduced tyrosyl groups was performed by the Chloramine-T method. The labeling efficiency of the BHR-treated **liposome conjugate** was high in comparison with that of the BHR-untreated **liposome conjugate.** An in vitro inhibition study showed that the binding affinity of 125I-labeled BHR-treated GCL (125I-F3S-BH) with lectin was twice as high as that of untreated **conjugate** (125I-F3S). The biodistribution of 125I-F3S-BH in mice was considerably different from that of 125I-F3S. 125I-F3S-BH was more rapidly taken up by

the liver and was more rapidly excreted from the liver than 125I-F3S. Moreover, 125I-F3S-BH accumulated more rapidly into the kidneys, which resulted a lower radioactivity in the blood circulation at an earlier time point than in the case of 125I-F3S. The characteristics of tumor accumulation of 125I-F3S-BH and 125I-F3S were similar to those in blood. If F3S is to be employed as an in vivo targeting ligand in biodistribution studies, BHR would be a suitable tool for radiolabeling because it allows GCL to retain the biological activity and characteristics of the unmodified **conjugate.**

L16 ANSWER 30 OF 179 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

2002153572 EMBASE Change in pharmacokinetic and pharmacodynamic behavior of gemcitabine in human tumor xenografts upon entrapment in vesicular phospholipid gels. Moog R.; Burger A.M.; Brandl M.; Schuler J.; Schubert R.; Unger C.; Fiebig H.H.; Massing U.. U. Massing, Tumor Biology Center, Department of Clinical Research, Breisacher Strasse 117, 79106 Freiburg, Germany. umas@tumorbio.uni-freiburg.de. Cancer Chemotherapy and Pharmacology 49/5 (356-366) 2002.
Refs: 39.
ISSN: 0344-5704. CODEN: CCPHDZ. Pub. Country: Germany. Language: English. Summary Language: English.

AB Purpose: The in vivo pharmacokinetics (PK), biodistribution and antitumor activity of a new liposomal formulation of gemcitabine (GemLip) were compared to the conventional (clinical) formulation of gemcitabine (GemConv). Methods: Gemcitabine was entrapped in a vesicular phospholipid gel (VPG) consisting of densely packed liposomes. Redispersed VPG containing GemLip consisted of 33% liposomally entrapped and 67% free gemcitabine. The in vivo efficacies of GemLip and GemConv were compared using the subcutaneously growing human soft tissue sarcoma SXF 1301 and the orthotopically growing human bladder cancer BXF 1299T. PK and biodistribution were evaluated using radiolabeled drug and lipid in SXF 1301 tumor-bearing nude mice. Results: GemLip was highly active in SXF 1301 at a gemcitabine dose of 6-9 mg/kg (days 1, 8 and 15; dose near the MTD). In the 6-mg/kg groups, complete tumor remissions were observed in seven of eight mice. Equimolar doses of GemConv resulted in only moderate tumor growth inhibition. Even at equitoxic doses (360 mg/kg given on days 1, 8 and 15, or 120 mg/kg on days 1, 5 and 8) GemConv was less active than GemLip. Furthermore, GemLip was active in the orthotopically growing BXF 1299T bladder cancer model at 6 mg/kg and prevented distant organ metastasis. In the PK study, GemLip achieved a 35-fold higher plasma AUC (1680 mg.ovrhdot.h/ml) than GemConv (47.6 mg.ovrhdot.h/ml). The serum half-lives were 0.15 h for free gemcitabine and 13.3 h for liposomal gemcitabine (6 mg/kg each i.v.). Moreover, gemcitabine levels in tumors were fourfold higher following injection of GemLip than following injection of GemConv. Conclusions: GemLip is a highly effective gemcitabine delivery system which results in superior gemcitabine pharmacodynamics and PK than GemConv. The enhanced in vivo efficacy might be explained by sustained release and passive tumor targeting.

L16 ANSWER 31 OF 179 MEDLINE on STN DUPLICATE 9

2002720816. PubMed ID: 12483036. Selective inhibition of systemic anti-OVA IgE production in response to oral pre-treatment with OVA-**liposome conjugates.** Naito Seishiro; Taneichi Maiko; Kato Hiroshi; Tanaka Yuriko; Ami Yasushi; Suzaki Yuriko; Mori Masahito; Nakano Yoshio; Yamamura Hiroyuki; Morokuma Kazunori; Ohkuma Kunio; Miyake Hidekazu; Kiniwa Mamoru; Komuro Katsutoshi; Uchida Tetsuya. (Department of Safety Research on Blood and Biological Products, National Institute of Infectious Diseases, Musashimurayama, Tokyo, Japan.) International archives of allergy and immunology, (2002 Dec) 129 (4) 314-9. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB BACKGROUND: We have previously reported that intraperitoneal injection with OVA-**liposome conjugates** induces OVA-specific and IgE-selective unresponsiveness in mice. METHODS: In the present study, the effects of oral pre-treatment with OVA-**liposome**

conjugates or with plain OVA solution on anti-OVA IgG antibody production were investigated in mice after subsequent immunization with alum-adsorbed OVA. Control mice received only the immunization. RESULTS: The levels of serum anti-OVA IgG antibody in mice receiving oral administration of OVA-liposome were comparable to those in the control mice. However, in mice receiving oral administration of the same dose of plain OVA, levels of serum anti-OVA IgG antibody were significantly lower than those in control mice. Surprisingly, anti-OVA IgE antibody production was completely inhibited in mice receiving oral administration of OVA-**liposome conjugates.** Splenic CD4(+) T cells of mice receiving oral administration of OVA-liposome and those of control mice produced comparable levels of cytokines, while those of mice receiving oral administration of plain OVA solution produced significantly lower levels of cytokines than those in the other two groups. CONCLUSION: Orally administered OVA-liposome did not affect anti-OVA IgG production but did inhibit anti-OVA IgE antibody production, while orally administered OVA solution inhibited production of both IgG and IgE antibodies. These results suggest that antigen-**liposome conjugates** can possibly be orally administered in order to control antigen-specific IgE antibody production, without affecting IgG antibody production.

L16 ANSWER 32 OF 179 MEDLINE on STN DUPLICATE 10
2002280416. PubMed ID: 12021548. Protection of monkeys against Shiga toxin induced by Shiga toxin-**liposome conjugates.** Suzaki Yuriko; Ami Yasushi; Nagata Noriyo; Naito Seishiro; Kato Hiroshi; Taneichi Maiko; Takahashi Motohide; Komiya Takako; Satoh Sachihiro; Gondaira Fumio; Sugiyama Junichi; Nakano Yoshio; Mori Masahito; Komuro Katsutoshi; Uchida Tetsuya. (Division of Experimental Animals Research, Department of Safety Research on Biologics, National Institute of Infectious Diseases, 4-7-1 Gakuen, Musashimurayama, Tokyo 208-0011, Japan.) International archives of allergy and immunology, (2002 Apr) 127 (4) 294-8. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.
AB BACKGROUND: We previously reported that the purified Shiga toxins (Stx) Stx1 and Stx2, when coupled with liposomes, induced substantial production of anti-Stx1 and anti-Stx2 IgG antibody, respectively, in mice. The levels of anti-Stx antibody in the sera of mice immune to Stx-liposome correlated well with the protection against subsequent challenge with Stx. Furthermore, mice immunized with a mixture of Stx1-liposome and Stx2-liposome were successfully protected against oral infection with cytotoxin-producing Escherichia coli O157:H7. METHODS: In this study, the induction of protection against Stx2 by Stx2-liposomes was evaluated in monkeys. RESULTS: Stx2-liposomes induced a substantial amount of anti-Stx2 IgG antibodies as well as Stx2 neutralizing antibodies in monkeys. Test monkeys were successfully protected against challenge with lethal doses of Stx2. Moreover, these monkeys showed no apparent symptoms, while nonimmunized control monkeys died within 4 days with hemorrhagic gastroenteritis and renal disorder. In addition, as shown by other cases involving antigen-**liposome conjugates**, Stx2-liposome did not induce anti-Stx2 IgE antibody production, though it stimulated the production of a substantial amount of anti-Stx2 IgG antibodies. CONCLUSION: These results suggest that Stx-**liposome conjugates** may serve as candidate vaccines to induce protection against death caused by cytotoxin-producing E. coli infection.

L16 ANSWER 33 OF 179 EMBASE on STN
2002144007 EMBASE Liposomal encapsulation enhances antiviral efficacy of SPC3 against human immunodeficiency virus type-1 infection in human lymphocytes. De Mareuil J.; Mabrouk K.; Doria E.; Moulard M.; De Chasteigner S.; Oughideni R.; Van Rietschoten J.; Rochat H.; De Waard M.; Sabatier J.-M.. J.-M. Sabatier, CNRS UMR 6560, Laboratoire de Biochimie, Faculte de Medecine Secteur Nord, 13916 Marseille Cedex 20, France.

sabatier.jm@jean-roche.univ-mrs.fr. Antiviral Research 54/3 (175-188) 2002.
Refs: 47.
ISSN: 0166-3542. CODEN: ARSRDR.
Publisher Ident.: S 0166-3542(02)00002-5. Pub. Country: Netherlands.
Language: English. Summary Language: English.

AB Because encapsulation of antiviral drugs in liposomes resulted generally in improved activity against retroviral replication in vivo, the antiviral effects of free-SPC3 and liposome-associated SPC3 were compared in cultured human lymphocytes infected with HIV-1. SPC3 was entrapped in various liposomal formulations, either different in size (mean diameter of 100 and 250 nm), SPC3 concentration or cholesterol content. Liposome-associated SPC3 were tested for both inhibition of cell-cell fusion and infection with HIV-1 clones. SPC3 inhibited HIV-1-induced fusion at a micromolar concentration range. When associated with liposomes, SPC3 was found to be about 10-fold more potent than free SPC3 in inhibiting syncytium formation. Continuous treatment with free SPC3 also inhibited virus production in a dose-dependent manner, with inhibition of HIV infection of C8166 T-cells or human peripheral blood lymphocytes (PBLs) at micromolar concentrations. Liposomal entrapment was found to increase the antiviral efficacy of SPC3 by more than 10- and 5-fold in C8166 and PBLs, respectively. These data suggest that the liposome approach may be used to improve SPC3 antiviral efficacy.

L16 ANSWER 34 OF 179 EMBASE on STN

2002077793 EMBASE Pharmacokinetic comparison of intravenous carbendazim and remote loaded carbendazim liposomes in nude mice. Jia L.; Garza M.; Wong H.; Reimer D.; Redelmeier T.; Camden J.B.; Weitman S.D.. L. Jia, Institute for Drug Development/CTRC, 14960 Omicron Drive, San Antonio, TX 78245-3217, United States. ljia@saci.org. Journal of Pharmaceutical and Biomedical Analysis 28/1 (65-72) 1 Apr 2002.
Refs: 17.
ISSN: 0731-7085. CODEN: JPBADA.
Publisher Ident.: S 0731-7085(01)00702-6. Pub. Country: Netherlands.
Language: English. Summary Language: English.

AB Carbendazim is a novel anticancer agent. The aim of this study was to prepare and characterize a remote loaded liposome preparation of carbendazim, and compare its pharmacokinetic profile to that of unencapsulated carbendazim. Carbendazim was encapsulated in liposomes composed of sphingomyelin-cholesterol (3:1, w/w) by remote loading in response to a transmembrane pH gradient (pH 0.5 in/pH 4.0 out), which resulted in encapsulation of more than 95% of the available drug in preformed vesicles. High drug/lipid ratios were prepared which correspond to a molar ratio of up to 0.8. Physical isolation of the free drug and dialysis were used to determine the in vitro release of carbendazim from liposomes. The release was independent of the initial drug/lipid ratio and choice of internal buffer composition. Liposomal carbendazim (200 mg kg(-1)) was intravenously administered to athymic nude mice and the serum levels of free carbendazim were determined by HPLC analysis after a methanol-induced protein precipitation. Administration of liposomal carbendazim to mice resulted in significant alterations in the pharmacokinetics. Serum levels of free carbendazim were approximately 10-fold greater than those achieved for the same dose of unencapsulated drug. Liposomal carbendazim showed both high C(max), AUC and low clearance rate. Liposomal carbendazim and unencapsulated carbendazim displayed a similar terminal half-life (43-48 min). The relatively large volume of distribution of carbendazim suggests that the compound may partially enter cells or be bound to some extravascular structures. The results indicate that the liposomal formulation of carbendazim significantly increases its blood concentrations.

L16 ANSWER 35 OF 179 BIOSIS on STN

2002:597509 Document No.: PREV200200597509. Tumor targeted drug delivery directed to radiation-induced cell adhesion molecules in tumor vascular endothelium. Geng, L. [Reprint author]; Konjeti, S. R. [Reprint author]; Onishko, H. [Reprint author]; Hallahan, D. E. [Reprint author]. Department of Radiation Oncology, Vanderbilt University, Nashville, TN, USA. International Journal of Radiation Oncology Biology Physics, (2002) Vol. 54, No. 2 Supplement, pp. 27. print.
Meeting Info.: 44th Annual Meeting of the American Society for Therapeutic Radiology and Oncology. New Orleans, LA, USA. October 06-10, 2002. American Society for Therapeutic Radiology and Oncology; International Society of Radiation Oncology.
CODEN: IOBPD3. ISSN: 0360-3016. Language: English.

L16 ANSWER 36 OF 179 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
2001:408313 Document No.: PREV200100408313. Liposome-enhanced immunoassay and test device. Durst, Richard Allen [Inventor]; Reeves, Stuart Graham [Inventor, Reprint author]; Siebert, Sui Ti Atienza [Inventor]. Geneva, NY, USA. ASSIGNEE: Cornell Research Foundation, Inc.. Patent Info.: US 6248596 June 19, 2001. Official Gazette of the United States Patent and Trademark Office Patents, (June 19, 2001) Vol. 1247, No. 3. e-file.
CODEN: OGUPE7. ISSN: 0098-1133. Language: English.
AB A test device for detecting or determining an analyte in a test solution includes an absorbent material having separate contact, competitive binding, and measurement portions. The contact portion is positioned for contact with and uptake of the test solution. The competitive binding portion has a binding material for the analyte non-diffusively bound thereto. The measurement portion has a receptor for the analyte and marker-encapsulating liposomes non-diffusively bound thereto. In a method for using the test device, a solution containing the analyte and the analyte-**liposome conjugate** is allowed to traverse the absorbent material from the contact portion through the competitive binding portion and on through the measurement portion of the absorbent material. The amount of marker in the measurement portion of the absorbent material, following traversal by the test solution, is then determined as a measure of the analyte in the sample. Liposomes encapsulating an electroactive marker are used in conjunction with a test device as described above but which includes an electrochemical measurement portion in place of the measurement portion described above. Test devices and methods employing electrochemical detection or quantification of an electroactive marker corresponding to the amount of analyte in a sample may be either amperometric or potentiometric.

L16 ANSWER 37 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2001:265463 Document No. 134:294521 IL13 mutants. Debinski, Waldemar; Thompson, Jeffrey P. (The Penn State Research Foundation, USA). PCT Int. Appl. WO 2001025282 A1 20010412, 81 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English).
CODEN: PIXXD2. APPLICATION: WO 2000-US27567 20001005. PRIORITY: US 1999-PV157934 19991006.
AB This invention provides mutant human interleukin 13 mols. showing varying specificity for the restricted (IL4 independent) IL13 receptor. The mutant hIL13 mols. include those made by substituting the amino acid residues that occur in the alpha-helix regions of native hIL13 with various other amino acid residues. Some of the mutants retain the ability to bind and cause signaling through IL13 receptors, while other mutants do not. These mutants may be useful for therapy of interleukin 13-related diseases, e.g. inflammation, asthma or allergy.

L16 ANSWER 38 OF 179 MEDLINE on STN DUPLICATE 11

2001435655. PubMed ID: 11337529. An analytic dosimetry study for the use of radionuclide-**liposome conjugates** in internal radiotherapy. Emfietzoglou D; Kostarelos K; Sgouros G. (Department of Medical Physics, University of Ioannina Medical School, Ioannina, Greece.) Journal of nuclear medicine : official publication, Society of Nuclear Medicine, (2001 Mar) 42 (3) 499-504. Journal code: 0217410. ISSN: 0161-5505. Pub. country: United States. Language: English.

AB A dosimetric analysis has been performed to evaluate the potential of liposome systems as carriers of radionuclides in internal radiotherapy. METHODS: Pharmacokinetic data for a variety of liposome constructs (multilamellar vesicles [MLV]; small unilamellar vesicles [SUV]; and sterically stabilized liposomes, monosialoganglioside [G(M1)]-coated) were used to obtain tumor and normal-organ absorbed dose estimates for (67)Cu, (188)Re, (90)Y, and (131)I. Dosimetry was performed for two tumor models: subcutaneous Ehrlich ascites tumor, growing intramuscularly, and C26 colon carcinoma, growing intrahepatically. Dose estimates were obtained using the MIRD schema. Tumor doses were obtained assuming local deposition of electron energy; photon contributions were incorporated assuming spheric tumor geometry. With the conservative assumption that intravenously administered liposomes achieve rapid equilibration with the red marrow extracellular fluid volume, red marrow absorbed dose estimates were obtained from blood kinetics. RESULTS: For intramuscular tumors, absorbed dose ratios for tumor to red marrow ranged from 0.93 ((131)I-MLV) to 13.9 ((90)Y-SUV). Tumor-to-liver ratios ranged from 0.08 ((188)Re-MLV) to 0.92 ((188)Re-SUV); corresponding values for tumor to spleen were 0.13 ((90)Y-MLV) and 0.54 ((188)Re-G(M1)). The optimal combination of radionuclide and liposome system was obtained with (90)Y-SUV. Tumor-to-liver ratios for the G(M1)-coated construct were greatest when the tumor was intrahepatic (1.13 for (90)Y). For a given liposome system, absorbed dose ratios for tumor to normal tissue exhibited up to a twofold variation depending on the radionuclide selected. CONCLUSION: This study provides a dosimetric evaluation for the use of some liposome systems as carriers in targeted radionuclide therapy. Although much further work must be undertaken before any clinical application is considered, these results suggest that radionuclide targeting using liposomes is feasible and may have the advantage of reduced red marrow absorbed dose.

L16 ANSWER 39 OF 179 MEDLINE on STN DUPLICATE 12

2002010557. PubMed ID: 11353537. Surface-linked liposomal antigen induces ige-selective unresponsiveness regardless of the lipid components of liposomes. Nakano Y; Mori M; Nishinohara S; Takita Y; Naito S; Kato H; Taneichi M; Komuro K; Uchida T. (NOF Corporation, Tsukuba Research Laboratory, Ibaraki, Japan.) Bioconjugate chemistry, (2001 May-Jun) 12 (3) 391-5. Journal code: 9010319. ISSN: 1043-1802. Pub. country: United States. Language: English.

AB We have previously reported that antigen coupled with liposomes induced antigen-specific and IgE-selective unresponsiveness in mice. This antigen preparation was investigated for application in a novel vaccine protocol to induce minimal IgE synthesis. In this study, ovalbumin (OVA)-**liposome conjugates** were made using liposomes of four different lipid components, including unsaturated carrier lipid and three different saturated carrier lipids, after which the induction of anti-OVA antibody production was investigated in mice. All of the OVA-**liposome conjugates** induced IgE-selective unresponsiveness. The membrane fluidity of liposomes, as measured by detecting changes in the fluorescence polarization of a 1,6-diphenyl-1,3,5-hexatriene (DPH) probe located in the bilayers, was significantly higher in liposomes consisting of unsaturated carrier lipids than those of the other liposomes consisting of saturated carrier lipids. The highest titer of anti-OVA IgG was observed in mice immunized with OVA-liposomes made using liposomes consisting of unsaturated carrier lipids. In addition, among these OVA-liposomes, the one possessing the longest carbon chain induced the lowest IgG antibody production. These results suggest that the membrane fluidity of liposomes might affect the adjuvant effect of liposomes but not the induction of IgE-selective

unresponsiveness in immunizations with surface-linked liposomal antigens.

L16 ANSWER 40 OF 179 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE 13

2001:731795 The Genuine Article (R) Number: 470XU. Preparation and characterization of neoglycoprotein-**liposome conjugates** : A promising approach to developing drug delivery materials applying sugar chain ligands. Yamazaki N (Reprint); Jigami Y; Gabius H J; Kojima S . Natl Inst Adv Ind Sci & Technol, Nanotechnol Res Inst, Tsukuba, Ibaraki 3058565, Japan; Natl Inst Adv Ind Sci & Technol, Inst Mol & Cell Biol, Tsukuba, Ibaraki, Japan; Univ Munich, Inst Physiol Chem, D-8000 Munich, Germany; Sci Univ Tokyo, Fac Pharmaceut Sci, Tokyo 162, Japan. TRENDS IN GLYCOSCIENCE AND GLYCOTECHNOLOGY (MAY 2001) Vol. 13, No. 71, pp. 319-329. Publisher: FCCA-FORUM CARBOHYDRATES COMING AGE. C/O GAKUSHIN PUBLISHING CO LTD 1-1-8 TARUMI-CHO, SUITA 564-0062, OSAKA, 30015, JAPAN. ISSN: 0915-7352 . Pub. country: Japan; Germany. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB To translate the emerging insights into the functionality of the sugar code into applications in organic materials science, we have paid special attention to carbohydrate-protein(lectin) interactions. They are increasingly delineated to play an important role in biological recognition systems. Thus, the custom-made design of research tools and the examination of how to practically exploit them are becoming burgeoning research areas for producing new functional materials. We here report preparation and characterization of novel types of neoglycoprotein-**liposome conjugates**, and indicate applications by studying recognition functions of these tailored carriers with defined sugar part as the recognition function using a model system and in vivo experiments. Various types of neoglycoprotein-**liposome conjugates** were prepared according to a method including preparation of mixed micelles and then of liposomes, chemical coupling of neoglycoproteins to the characterized liposomes, and further sequential enzymatic glycosylation to refine the glycan part. The assays indicated carbohydrate-specific recognition functions of these neoglycoprotein-**liposome conjugates.** Monitoring of tissue distribution using Ehrlich solid tumor-bearing mice showed individual response of diverse tissues towards various types of applied neoglycoprotein-**liposome conjugates** harboring a series of sugar chain ligands including mono- and oligosaccharides. This type of carbohydrate-conjugated material is expected to find applications in basic glycoscientific research as well as in applied areas such as tissue-specific drug targeting materials.

L16 ANSWER 41 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

2001:688272 Document No. 137:98771 Targeting polymerized liposome vaccine carriers to intestinal M cells. Ann Clark, M.; Blair, H.; Liang, L.; Brey, R. N.; Brayden, D.; Hirst, B. H. (Department of Physiological Sciences, Medical School, University of Newcastle, Newcastle upon Tyne, NE2 4HH, UK). Vaccine, 20(1-2), 208-217 (English) 2001. CODEN: VACCDE. ISSN: 0264-410X. Publisher: Elsevier Science Ltd..

AB Due to their transcytotic capability, intestinal M cells may represent an efficient potential route for oral vaccine delivery. The authors previously demonstrated that the lectin Ulex europaeus agglutinin 1 (UEA1, specific for α-l-fucose residues) selectively binds to mouse Peyer's patch M cells and targets 0.5 μm polystyrene microparticles to these cells. Using a gut loop model, the authors now demonstrate that covalently-membrane-bound UEA1 similarly targets polymerized liposomes (Orasomes, approx. 200 nm diameter), potential biocompatible oral vaccine delivery vehicles, to mouse M cells. Targeting was inhibited by α-l-fucose while the co-entrapped adjuvant, monophosphoryl Lipid A (MPL), failed to exert any detrimental effect on UEA1-mediated M cell targeting. Lectin-mediated M cell targeting may thus permit the efficacy of mucosal vaccines to be enhanced if cellular relationship between particle binding and immune outcome can be established.

L16 ANSWER 42 OF 179 MEDLINE on STN DUPLICATE 14
2001407391. PubMed ID: 11458505. The monoclonal antibody W7C5 defines a novel surface antigen on hematopoietic stem cells. Giesert C; Almeida-Porada G; Scheffold A; Kanz L; Zanjani E D; Buhring H J. (Department of Hematology and Oncology, University of Tubingen, 72076 Tubingen, Germany.) Annals of the New York Academy of Sciences, (2001 Jun) 938 175-83. Journal code: 7506858. ISSN: 0077-8923. Pub. country: United States. Language: English.

AB We recently raised a monoclonal antibody, termed W7C5, against a surface antigen that is expressed at low levels on bone marrow and peripheral blood CD34+ stem/progenitor cells but at high levels on fetal liver CD34+ cells. A reasonable staining intensity was achieved using magnetofluorescent **liposome conjugates** to analyze expression of W7C5 antigen on CD34+CD38- bone marrow (BM) cells. Flow cytometric analyses revealed that W7C5 detects about 50% of immature CD34+CD38- BM cells that coexpressed the differentiation antigens CD164, CD133, and CD172a (SIRP alpha). In addition, W7C5 also recognized a CD34- BM fraction. These cells were negative for CD117 and CD133, but expressed CD45 and moderate levels of CD164. Injection of selected CD34+W7C5+ and CD34-W7C5+ cells into 55-60-day-old fetal sheep resulted in an engraftment of both fractions. Partial amino acid sequence analysis of affinity-purified lysates of KU-812 cells revealed that W7C5 detects a novel membrane protein. Together, W7C5 defines a novel molecule that is expressed on CD34+ as well as on CD34- stem cell subsets.

L16 ANSWER 43 OF 179 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 15
2000:373589 Document No.: PREV200000373589. Glycosylated protein-**liposome conjugates** and methods for their preparation. Ansell, Steven Michial [Inventor, Reprint author]. Vancouver, Canada. ASSIGNEE: Inex Phamaceuticals Corp., Burnaby, Canada. Patent Info.: US 6027726 February 22, 2000. Official Gazette of the United States Patent and Trademark Office Patents, (Feb. 22, 2000) Vol. 1231, No. 4. e-file. CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

AB The present invention provides glycosylated protein-liposome compositions which are useful for the targeted delivery of a therapeutic agent. The compositions contain an oxidized protein, typically an antibody, which is covalently attached to a lipid by means of a crosslinking agent having an acid hydrazide functionality on one terminus and a sulfhydryl functionality on the other terminus. The lipid is present in a liposome formulation. Methods for preparing the compositions are also provided. In the methods, a glycosylated protein is first oxidized then reacted with a lining group having an acid hydrazide on one end and a sulfhydryl or protected sulfhydryl group on the other end. The resultant modified protein is then reacted with a liposome formulation of a lipid having a sulfhydryl reactive functional group to covalently attach the protein to the liposome.

L16 ANSWER 44 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2000:772487 Document No. 133:340248 **Conjugate** having a cleavable linkage for use in a liposome. Zalipsky, Samuel; Gabizon, Alberto A. (Alza Corporation, USA; Hadasit Medical Research Services & Development Ltd.). PCT Int. Appl. WO 2000064484 A2 20001102, 60 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US10922 20000421. PRIORITY: US 1999-PV130897 19990423.

AB **Conjugates** of a hydrophobic moiety, such as a lipid, linked through a cleavable dithiobenzyl linkage to a therapeutic agent are described. The dithiobenzyl linkage is susceptible to cleavage by mild

thiolysis, resulting in release of the therapeutic agent in its original form. The linkage is stable under nonreducing conditions. The **conjugate** can be incorporated into liposomes for administration in vivo and release of the therapeutic agent in response to endogeneous in vivo reducing conditions or in response to administration of an exogenous reducing agent. P-diacyldiglyceroldithiobenzal-mitomycin C was prepared, and combined with hydrogenated soy phosphatidylcholine (HSPC) and distearoyl phosphatidylethanolamine derivatized with methoxy polyethylene glycol (mPEG-DSPE) in a molar ratio of 5/90/5, and dissolved in ethanol to obtain a liposome formulation and for its pharmacokinetic study in vivo.

L16 ANSWER 45 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2000:772486 Document No. 133:340247 Releasable linkage and compositions containing same. Zalipsky, Samuel (Alza Corporation, USA). PCT Int. Appl. WO 2000064483 A2 20001102, 63 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US10830 20000421. PRIORITY: US 1999-PV130897 19990423.

AB A compound comprised of a hydrophilic polymer covalently yet reversibly linked to an amine-containing ligand through a dithiobenzyl linkage is described. O- and p-methoxy polyethylene glycol-urethane-ethyldithiobenzyl-distearoylphosphatidyl ethanolamine were prepared and combined with dioleoyl phosphatidylehtanolamine (DOPE) to obtain liposomes having an average diameter of 100 nm.

L16 ANSWER 46 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2000:592499 Document No. 133:187950 NG2/HM proteoglycan-binding peptides that home to angiogenic vasculature and related methods. Burg, Michael A.; Pasqualini, Renata; Arap, Wadih; Ruoslahti, Erkki I.; Stallcup, William B. (Burnham Institute, USA). PCT Int. Appl. WO 2000048464 A1 20000824, 86 pp. DESIGNATED STATES: W: JP; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US3864 20000216. PRIORITY: US 1999-250700 19990216.

AB The present invention provides angiogenic vasculature homing mols. that bind to NG2/HM proteoglycan, including, for example, a peptide comprising the amino acid sequence TAASGVRSMH (SEQ ID NO:1) or LTLRWVGLMS (SEQ ID NO:2). The invention also provides **conjugates** comprising an angiogenic vasculature homing mol. linked to a moiety such as a drug, a cytotoxic agent, a chemotherapeutic agent, or a detectable agent. The invention addnl. provides a method of targeting angiogenic vasculature in a tumor in vivo by contacting the angiogenic vasculature with an angiogenic vasculature homing mol. that selectively homes to a NG2/HM proteoglycan, wherein the angiogenic vasculature homing mol. is not an antibody. The invention addnl. provides a method of inhibiting angiogenesis in a tumor of a subject by administering to the subject a **conjugate** comprising a moiety linked to an angiogenic vasculature homing mol. that selectively binds a NG2/HM proteoglycan, wherein the angiogenic vasculature homing mol. is not an antibody.

L16 ANSWER 47 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2000:493393 Document No. 133:115101 Methods for inhibiting tumor metastasis, and selectin-binding peptides useful therefor. Fukuda, Michiko; Fukuda, Minoru (The Burnham Institute, USA). PCT Int. Appl. WO 2000041711 A1 20000720, 76 pp. DESIGNATED STATES: W: JP, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US1012 20000114. PRIORITY: US 1999-232484 19990115.

AB In accordance with the present invention, there are provided peptides that

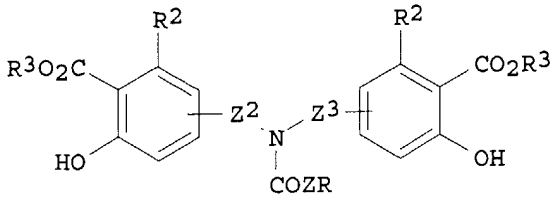
bind to a member of the mammalian selectin family and inhibit the binding of a carbohydrate to the selectin. Invention peptides are useful to inhibit the adhesion of cells containing particular cell-surface carbohydrates to cells containing cell-surface selectins. Also provided are pharmaceutical compns. comprising invention peptides useful in methods for inhibiting a carbohydrate from binding to a selectin, and in methods of inhibiting tumor cell metastasis in a subject. Peptide IELLQAR multivalent (Fmoc eight branch) prevented metastasis of melanoma B16 cells in mice.

L16 ANSWER 48 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2000:116860 Document No. 132:171073 **Conjugates** targeted to target receptors and/or interleukin-2 receptors. Prakash, Ramesh K.; Clemens, Christopher M. (Watson Laboratories, Inc., USA). PCT Int. Appl. WO 2000007543 A2 20000217, 67 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US17648 19990804. PRIORITY: US 1998-128572 19980804.

AB A composition for intracellular delivery of a chemical agent into a target receptor and/or interleukin-2-receptor-bearing cell, e.g. an activated T cell and cancer cell, includes a chemical agent, at least one copy of target-receptor binding and/or an interleukin-2-receptor-binding and endocytosis-inducing ligand coupled to a water soluble polymer. The ligand binds to a target receptor and/or IL-2 receptor on the target receptor and/or IL-2-receptor-bearing cell and elicits endocytosis of the composition The composition also optionally includes a biodegradable spacer for coupling the chemical agent and the ligand to the polymer. Chemical agents can include cytotoxins, transforming nucleic acids, gene regulators, labels, antigens, drugs, and the like. A preferred water soluble polymer is polyalkylene oxide, such as polyethylene glycol and polyethylene oxide, and activated derivs. thereof. The composition can further comprise a carrier such as another water soluble polymer, liposome, or particulate. Methods of using these compns. for delivering a chemical agent in vivo or in vitro are also disclosed. A method of detecting a disease, such as cancer, T-cell lymphocytic leukemia, T-cell acute lymphoblastic leukemia, peripheral T-cell lymphoma, Hodgkin's disease, and non-Hodgkin's lymphoma, associated with elevated levels of soluble target receptor and/or IL-2 receptor is also disclosed.

L16 ANSWER 49 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2000:855780 Document No. 134:29208 Preparation of reagents suitable for the modification of a bioactive species for the purpose of incorporating a bifunctional boronic compd. complexing moiety for subsequent conjugation to bioactive species.. Ahlem, Clarence N.; Kaiser, Robert J.; Lund, Kevin P.; Stolowitz, Mark L. (Prolinx, Inc., USA). U.S. US 6156884 A 20001205, 40 pp., Cont.-in-part of U.S. 5,877,297. (English). CODEN: USXXAM. APPLICATION: US 1998-222468 19981229. PRIORITY: US 1996-691930 19960805; US 1996-689283 19960805; US 1997-956196 19971022; US 1997-956194 19971022.

GI



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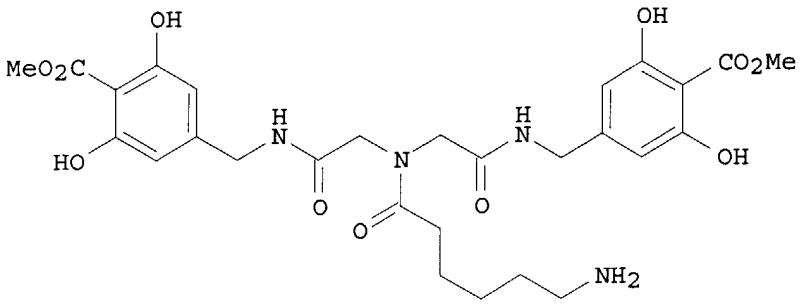


II

AB Title reagents [I; R = electrophilic or nucleophilic moiety suitable for reaction with a biol. active species; R2 = H, OH; R3 = alkyl, methylene bearing an electroneg. substituent; Z = (CH2)n, CH2O(CH2CH2O)n2; n = 1-5; n2 = 1-4; Z2, Z3 = CH2, CH2CONHCH2, CH2CONH(CH2)n3, CONHCH2, (CH2)n4NHCO(CH2)n5CONHCH2; n3 = 1-5; n4 = 2, 3; n5 = 1-4], were prepared (no data). Thus, 2-[6-[(tert-butoxy)carbonylamino]-N-(carboxymethyl)hexanoylamino]acetic acid in DMF was treated with N-hydroxysuccinimide and DCC followed by 16 h stirring; Me 4-(aminomethyl)-2,6-dihydroxybenzoic acid hydrochloride (preparation given) and diisopropylethylamine in DMF were added followed by 8 h stirring to give 62% protected coupling product, which was stirred with CF3CO2H in CH2Cl2 to give 97% title compound (II) as the TFA salt.

L16 ANSWER 50 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2000:508917 Document No. 133:140227 Method and compositions for lipidization of hydrophilic molecules. Shen, Wei-chiang; Wang, Jinghua (The University of Southern California, USA). U.S. US 6093692 A 20000725, 34 pp. (English). CODEN: USXXAM. APPLICATION: US 1997-936898 19970925. PRIORITY: US 1996-PV77177 19960926; US 1997-PV49499 19970613.

AB Fatty acid derivs. of disulfide-containing compds. (for example, disulfide-containing peptides or proteins) comprising fatty acid-conjugated products with a disulfide linkage are employed for delivery of the compds. to mammalian cells. This modification markedly increases the absorption of the compds. by mammalian cells relative to the rate of absorption of the unconjugated compds., as well as prolonging blood and tissue retention of the compds. Moreover, the disulfide linkage in the **conjugate** is quite labile in vivo and thus facilitates intracellular or extracellular release of the intact compds. from the fatty acid moieties. N-palmityl-2-pyridyldithiocysteine was prepared and reacted with Bowman-Birk inhibitor (BBI) to obtain a palmityl disulfide **conjugate** of BBI. When the **conjugate** was incubated with colon carcinoma cells (Caco-2) in serum-free medium, the uptake of the **conjugate** was higher than that of BBI.

L16 ANSWER 51 OF 179 MEDLINE on STN DUPLICATE 16
2000510273. PubMed ID: 11062762. Tissue dosimetry of liposome-radionuclide complexes for internal radiotherapy: toward liposome-targeted therapeutic radiopharmaceuticals. Kostarelos K; Emfietzoglou D. (Weill Medical College of Cornell University-New York Presbyterian Hospital, NY 10021, USA.. kok2001@med.cornell.edu) . Anticancer research, (2000 Sep-Oct) 20 (5A) 3339-45. Journal code: 8102988. ISSN: 0250-7005. Pub. country: Greece.

Language: English.

AB BACKGROUND: Quantitative examination of the important physical parameters, such as the tumor absorbed dose and the tumor-to-normal-tissue (T-NT) absorbed dose ratios, for effective use of radionuclide-**liposome conjugates** m internal radiotherapy was carried out. METHODS: The Medical Internal Radiation Dose (MIRD) formalism was used to develop a set of dosimetric equations. Pharmacokinetic functions used as input information to the dosimetric model were derived from experimental time-biodistribution data. Multilamellar (MLV), small unilamellar (SUV) and sterically stabilized (GM1- and PEG-coated) liposomes were examined in combination with the very promising particle emitting radionuclides: 67Cu, 188Re and 211At. For comparative purposes, the widely used: 90Y and 131I were also included in the study. For all radionuclide-liposome combinations, the mean absorbed dose per amount of radioactivity administered was obtained: (i) for two different types of human xenografts located in the muscle and liver tissue, and (ii) for normal liver, spleen, kidneys, and total body. RESULTS: Regardless of radionuclide, the poorest values were obtained for the MLV liposomes. Due to more rapid uptake of sterically stabilized (GM,-coated) liposomes to the muscle tumor tissue as compared to SUVs, 211At and 188Re deliver higher tumor doses when combined with the former, while 67Cu, 90Y and 131I are more effective with SUVs. The most promising results were obtained for the [211At-GM1] complex in the liver tumor. CONCLUSION: The importance of liposome size and steric barrier when designing effective radionuclide-carrier systems was revealed, but most importantly the optimal matching between the radionuclide half-life and the time of maximum liposome accumulation ratio between the tumor and normal tissue.

L16 ANSWER 52 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

2000:672499 Document No. 134:152461 A model study using a series of fetuin-**liposome conjugates** bearing modified N-glycan ligands towards the development of glycoprotein-conjugated liposomal targeting carriers. Yamazaki, N.; Jigami, Y.; Kojima, S. (Department of Organic Materials, National Institute of Materials and Chemical Research, Higashi, 305-8565, Japan). Proceedings of the International Symposium on Controlled Release of Bioactive Materials, 27th, 1158-1159 (English) 2000. CODEN: PCRMEY. ISSN: 1022-0178. Publisher: Controlled Release Society, Inc..

AB A sequential enzymic approach was applied to prepare a series of fetuin-**liposome conjugates** exposing clustered N-glucan ligands on the liposomal membrane surface. In vitro lectin binding and in vivo biodistribution assays indicate that this series of liposomal prepns. is a promising tool for studying the function of N-glycans in drug targeting.

L16 ANSWER 53 OF 179 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 17

2000:472557 Document No.: PREV200000472557. Improvement of labeling efficiency of glycoprotein-**liposome conjugates** with iodine-125 by using Bolton-Hunter Reagent and their distribution in mice. Kawakita, Yasunori [Reprint author]; Yamazaki, Noboru; Kojima, Shuji [Reprint author]. Research Institute for Biological Sciences, Science University of Tokyo, 2669, Yamazaki, Noda-shi, Chiba Pref., 278-0022, Japan. Radioisotopes, (July, 2000) Vol. 49, No. 7, pp. 339-345. print. CODEN: RAISAB. ISSN: 0033-8303. Language: Japanese.

AB We have developed a new type of glycoprotein-**liposome conjugates** and examined their potential utilities as drug-targeting carriers which exploit cellular functions of carbohydrate-binding proteins, i.e. animal lectins. An extremely low labeling efficiency, however, has been often a big problem in biodistribution study by using radiolabeled glycoprotein-**liposome conjugates.** In this study, improvement of the labeling efficiency was conducted by using Bolton-Hunter Reagent (BHR). First, tyrosyl groups were introduced into liposome membrane through amines of a constitutive phospholipid, dipalmitoylphosphatidlethanolamine (DPPE). Then, glycoprotein-tyrosyl group introduced liposomes were iodinated with 125I

according to Chloramine-T methods. Labeling efficiency was markedly elevated in comparison with the BHR-untreated **liposome conjugates.** There was no significant changes in binding activity of BHR-treated glycoprotein-**liposome conjugates** with lectin. However biodistribution of glycoprotein-tyrosyl group introduced liposomes in mice was significantly different from the mother **conjugates.** Thus, another suitable method for radioiodination of the glycoprotein-**liposome conjugates** should be developed.

L16 ANSWER 54 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2000:503968 Document No. 133:159599 Study on the biodistribution of 99mTc-labeled paclitaxel liposome in xenograft-bearing nude mice. Zhang, Changying; Cheng, Wencai; Wang, Yanggong; Cui, Wuren; Zhao, Ming; Zhu, Xiaohua (Department of Obstetrics and Gynecology, Tongji Hospital, Tongji Medical University, Wuhan, 430030, Peop. Rep. China). Tongji Yike Daxue Xuebao, 29(3), 253-255 (Chinese) 2000. CODEN: TYDXEP. ISSN: 0258-2090. Publisher: Tongji Yike Daxue.

AB S.c. xenograft tumor model was established in 20 female nude mice. 99mTC-paclitaxel liposome (99mTc-TL) 0.2 mL was injected through tail vein into the mice. Five animals were killed in each time point of 15 min, 30 min, 90 min after injection. The major organs were taken out and accurately weighed including heart, liver, spleen, lung, kidney, intestine, uterus and appendix, skeleton and tumor tissue. The remaining 5 mice were subjected to the injection of 0.2 mL 99mTC-solution and killed 90 min after injection. Liver, spleen, lung and tumor tissue were taken out and weighed. γ-Measure device was used to measure the tissue radioactive intensity. Radioactive intensity was the highest (552.1±92.8 to 260.1±21.0 CPM/100 mg tissue) in spleen, liver and lung relatively, and tended to decrease with the prolongation of the time. The intensity in tumor tissue was obviously lower (3.6±0.6 CPM/100 mg tissue) but kept relative stabilization and did not show a decreasing tendency. There was statistically significant difference in radioactive intensity in liver, spleen and lung tissues ($P < 0.05$), but there was no significant difference in tumor tissue ($P > 0.05$) between 99mTC-TL group and 99mTC-solution group. Paclitaxel liposome after i.v. injection was mostly accumulated in liver, spleen, lung tissues in xenograft-bearing mice and showed a target ability. There was certain intensity in tumor tissue but it did not show target ability as compared with 99mTc-solution

L16 ANSWER 55 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2000:225011 Document No. 133:117036 Immunoliposome Sandwich Assay for the Detection of Escherichia coli O157:H7. Park, Sungsu; Durst, Richard A. (Department of Food Science and Technology, Cornell University, Geneva, NY, 14456-0462, USA). Analytical Biochemistry, 280(1), 151-158 (English) 2000. CODEN: ANBCA2. ISSN: 0003-2697. Publisher: Academic Press.

AB We describe the development of a field-portable colorimetric immunoassay for the detection of Escherichia coli O157:H7, using antibody-directed liposomes (immunoliposomes) encapsulating dye as an anal. reagent. Antibodies (anti-E. coli O157:H7) thiolated by 2-iminothiolane were coupled to maleimide-tagged liposomes encapsulating the marker dye, sulforhodamine B. TEM showed that the immunoliposomes bound only to the serotype without any cross-reactivity with tested neg. controls. A wicking reagent containing immunoliposomes and the test sample and a plastic-backed nitrocellulose strip with a measurement zone were used in a sandwich (noncompetitive) assay format. During the capillary migration of the wicking reagent, E. coli, with surface-bound immunoliposomes, was captured at the measurement zone on which antibodies to E. coli O157:H7 were immobilized. The color d. of the measurement zone was directly proportional to the amount of E. coli O157:H7 in the sample. The detection limit of the current assay with pure cultures of the serotype was .apprx.104 colony-forming units (CFU)/mL. The assay, which does not need washing and incubation steps, can be completed in 8 min. These results demonstrate the feasibility of using dye-encapsulating immunoliposomes in microporous membranes for the rapid detection of mols. with multivalent

antigenic sites. (c) 2000 Academic Press.

L16 ANSWER 56 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1999:460345 Document No. 131:88341 Polyamide oligomers and their use in drug delivery via liposomes. Ansell, Steven Michial (Inex Pharmaceuticals Corporation, Can.). PCT Int. Appl. WO 9933493 A1 19990708, 106 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-CA1185 19981222. PRIORITY: US 1997-113658 19971223; US 1998-73852 19980202.
AB Polyamide oligomers which can be conjugated to lipids, nucleic acids, peptides, proteins, etc., to form liposomes, virusomes, micelles, etc., optionally containing drugs or biol. agents, have the structure R[NR1(CH2CH2O)m(CH2)pCO(NHCHR2CO)q]nR3 [R = H, alkyl, acyl; each R1 = H, alkyl; or terminal NRR1 = N3; R2 = H, (un)substituted alkyl or aryl, amino acid side chain residue; R3 = H, halogen, OH, SH, alkoxy, NHNH2, NR4R5; R4, R5 = H, alkyl; m = 2-6; n = 4-80; p = 1-4; q = 0, 1]. Thus, tetraethylene glycol was monoetherified with dihydropyran, the resulting acetal etherified with BrCH2CO2Et and deprotected, and the terminal OH replaced by N3 to give N3(CH2CH2O)4CH2CO2Et, part of which was reduced to the NH2 derivative and part of which was hydrolyzed to the acid, after which the 2 products were condensed by use of dicyclohexylcarbodiimide to give N3(CH2CH2O)4CH2CONH(CH2CH2O)4CH2CO2Et. Two repetitions of this coupling procedure gave N3(CH2CH2O)4CH2CO[NH(CH2CH2O)4CH2CO]7OEt, which was saponified and converted to N3(CH2CH2O)4CH2CO[NH(CH2CH2O)4CH2CO]7NHCH2CH2OP(O)(OH)OCH2CH[O2C(CH2)16Me]CH2O2C(CH2)16Me.

L16 ANSWER 57 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1999:425791 Document No. 131:55532 Protein-binding peptides and their use in affinity chromatography, diagnosis and therapy. Ajoula, Harmesh Singh; Clarke, David John (Anmat Technology Limited, UK). PCT Int. Appl. WO 9932513 A1 19990701, 47 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-GB3855 19981221. PRIORITY: GB 1997-26956 19971219.
AB This invention relates to a protein-binding peptides not directly derived from a natural ligand binding protein known to bind protein, the protein-binding peptide comprising 2-30 amino acids and the uses of the polypeptide. Such peptides may be useful in affinity chromatog. because they are more stable to the harsh conditions used in this technique. The shortness of the peptides is advantageous in that the cost of producing them is less than that of protein-binding proteins. A peptide of the invention, GQVLQGAIKG, was found to bind strongly to peroxidase-labeled rabbit and goat IgG antibodies and native antibodies from a range of animal species, but not to the common enzymes used in labels in immunol. procedures.

L16 ANSWER 58 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1999:133618 Document No. 130:187175 **Conjugates** targeted to the interleukin-2 receptor. Prakash, Ramesh K. (Theratech, Inc., USA). PCT Int. Appl. WO 9907324 A2 19990218, 53 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG,

KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US16290 19980805. PRIORITY: US 1997-914042 19970805.

AB A composition for intracellular delivery of a chemical agent into an interleukin-2-receptor-bearing cell, e.g. an activated T cell, includes a chemical agent and at least two copies of an interleukin-2-receptor-binding and endocytosis-inducing ligand coupled to a water soluble polymer. The ligand binds to a receptor on the interleukin-2-receptor-bearing cell and elicits endocytosis of the composition The composition also optionally includes a spacer for coupling the chemical agent and the ligand to the polymer. Chemical agents can include cytotoxins, transforming nucleic acids, gene regulators, labels, antigens, drugs, and the like. A preferred water soluble polymer is polyalkylene oxide, such as polyethylene glycol and polyethylene oxide, and activated derivs. thereof. The composition can further comprise a carrier such as another water soluble polymer, liposome, or particulate. Methods of using these compns. for delivering a chemical agent in vivo or in vitro are also disclosed.

L16 ANSWER 59 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

1999:119837 Document No. 130:195756 **Conjugates** of polymers and antibodies specific for T lymphocytes, and their use as adjuvants. Chang, Tse Wen (Tanox Biosystems, Inc., USA). U.S. US 5872222 A 19990216, 6 pp., Cont.-in-part of U.S. Ser. No. 926.566, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1992-993291 19921218. PRIORITY: US 1991-688000 19910419; US 1992-819449 19920110; US 1992-926566 19920806.

AB Disclosed are **conjugates** including a substantially nonimmunogenic polymer backbone or microbead and binding mols., such as Fv, Fab, or F(ab')2 fragments of monoclonal antibodies or whole antibodies that are bound through their Fc carbohydrate moieties or have their Fc portion modified so that they cannot effect ADCC (antibody-dependent cellular cytotoxicity) or complement-mediated cytolysis, and that are specific for a T cell surface antigen, such as CD3, TCR, CD4, CD8, or CD28 on T cells. The polymer or microbead is preferably made of cross-linked dextran, ficoll, latex, or agarose, and is preferably of 0.1 to 10 μm in size, so that it can be suspended in fluids for in vivo applications. These **conjugates** can be used as adjuvants to enhance the antibody response against an administered immunogen.

L16 ANSWER 60 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

1999:362013 Document No. 131:1483 **Conjugate** for directed gene transfer. (IBFB Institut fuer Biomedizinische Forschung und Beratung G.m.b.H. i.G., Germany). Ger. Offen. DE 19752990 A1 19990602, 4 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1997-19752990 19971128.

AB A nonviral vector for directed gene transfer comprises a heterocyclic compound bound to a cell-specific protein (antibody, receptor, or ligand) conjugated directly or via a linker to a 2nd heterocyclic compound bound to a polycation which in turn binds a polyanionic nucleic acid sequence, preferably by condensation without steric hindrance. After selective binding of the antibody moiety to the target cells, the entire **conjugate** is pinocytosed by the cell and the nucleic acid is incorporated into the cell's genome. In another embodiment, a single heterocyclic residue with multiple hetero atoms is bound to both the protein ligand and the polycation-nucleic acid complex. This method shows greater cell selectivity than the use of viral vectors. Alternatively, the polycation may be replaced with a drug which is thereby targeted to a specific cell type.

L16 ANSWER 61 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

1999:722346 Document No. 132:313428 Liposome delivery of particle-emitting radionuclides for tumor radiotherapy. Emfietzoglou, D.; Kostarelos, K.; Stamatelou, M. (Division of Hematology, Greek Anticancer Institute, "Saint Savas" Oncology Hospital, Athens, 115 22, Greece). Proceedings of the International Symposium on Controlled Release of Bioactive Materials,

26th, 505-506 (English) 1999. CODEN: PCRMEY. ISSN: 1022-0178. Publisher: Controlled Release Society, Inc..

AB Radiation absorbed dose in liver tumor from various combinations of radionuclide-**liposome conjugates** was shown as well as tumor-to-whole-body ratio for the combinations.

L16 ANSWER 62 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

2000:252432 Document No. 133:79192 Synthesis, lectin-binding affinity, and biodistribution of novel neoglycoprotein-**liposome conjugates** bearing 6'-sialyl-n-acetyllactosamines and Lewis X trisaccharides. Yamazaki, Noboru; Kokubu, Tomokuni; Katsura, Tatsuo; Gabius, Hans-Joachim; Kojima, Shuji (Dep. Organic Materials, National Inst. Materials Chemical Res., Tsukuba, 305-8565, Japan). Drug Delivery System, 14(6), 498-505 (English) 1999. CODEN: DDSYEI. ISSN: 0913-5006. Publisher: Nippon DDS Gakkai Jimukyoku.

AB Carbohydrate-protein interactions have been reported to play an important role in various biol. processes such as cell-cell recognition, adhesion, and communication. This type of mol. interaction is attracting increasing interest in applied research areas such as cell type-specific targeting. Whereas a considerable level of expertise and experience to develop carbohydrate-mediated drug delivery systems based on glycolipid-bearing liposomes has been attained, the custom-made design and applications of glycoprotein-bearing liposomes are less explored. As a step to address this issue, we have developed a new type of neoglycoprotein-**liposome conjugates** in order to investigate their potential utility as drug-targeting devices which exploit cellular functions of carbohydrate-binding proteins, i. e. animal lectins. In the present study, we have employed a versatile chemoenzymic approach to synthesize a novel type of neoglycoprotein-**liposome conjugates** exposing clustered oligosaccharides on the membrane surface. In vitro lectin binding assay and in vivo biodistribution monitoring both indicate that this type of liposomal preparation with enzymically tailored carbohydrate chains is a promising tool warranting further efforts in drug-targeting research.

L16 ANSWER 63 OF 179 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 18

1999436031 EMBASE Liposomes as carriers of radionuclides: From imaging to therapy. Kostarelos K.; Emfietzoglou D.. K. Kostarelos, Department of Medicine, Cornell Univ. Weill Medical College, New York Presbyterian Hospital, 1300 York Avenue, New York, NY 10021, United States. kok2001@mail.med.cornell.edu. Journal of Liposome Research 9/4 (429-460) 1999.

Refs: 188.

ISSN: 0898-2104. CODEN: JLREE7. Pub. Country: United States. Language: English. Summary Language: English.

AB Liposomes have been studied quite extensively during the last twenty years or so as carriers for a variety of diagnostic molecules, in order to enhance the obtained in vivo target-to-background contrast, thus improve imaging resolution. In such applications, unlike chemotherapy and even more radiotherapy, low radiation doses are generally administered hence, apart from risk assessment purposes, the need for radiation dosimetry is not critical for their success. In the present article we will try to present and analyze critical factors that may affect any attempt to construct and investigate liposomes as carriers of particle-emitting radionuclides for radiotherapeutic purposes. Since dosimetric considerations for this kind of applications are considered essential for establishing radiotoxicity levels and dose-response relations for both healthy and tumor tissues, a description of current dosimetry methodologies will be included. It is aimed that the conceptual differences between imaging and therapy using radiolabeled **liposome conjugates**, along with those between chemotherapy and radiotherapy will be elucidated. The complex interplay of different pharmacokinetic (liposome biodistribution), physical (radionuclide half-life, particle emission characteristics),

physicochemical (liposome particle size, surface charge), and physiological (tumor dimensions, vasculature, pH) parameters will be qualitatively investigated towards optimal selection and design of liposome-radionuclide complexes.

L16 ANSWER 64 OF 179 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 19
1999326157 EMBASE Liposome-mediated delivery of radionuclides to tumor models for cancer radiotherapy: A quantitative analysis. Kostarelos K.; Emfietzoglou D.; Stamatelou M.. K. Kostarelos, Cornell University, Weil Medical College, Department of Medicine, 1300 York Avenue, New York, NY 10021, United States. Journal of Liposome Research 9/3 (407-424) 1999. Refs: 48.
ISSN: 0898-2104. CODEN: JLREE7. Pub. Country: United States. Language: English. Summary Language: English.
AB Towards the design of therapeutically effective liposome-radionuclide **conjugates**, the predominant focus should rest with the ability of such modalities to efficiently target tumor sites and thus selectively deliver cytotoxic levels of radiation doses. For this reason analytic dosimetric calculations were carried out to quantitatively examine the critical physical parameters for the potential clinical application of radionuclide-**liposome conjugates** in internal radiotherapy. The radiodosimetric model employed followed the mathematical formalism of the MIRD (Medical Internal Radiation Dose Committee) scheme. Analytic pharmacokinetic functions for a variety of liposome constructs coupled with the radiation properties of three of the most promising particle emitting radionuclides: Cu-67, Re-188, At-211 and the most widely used in the clinic I-131, were used as input information to the model developed. Results are presented in the form of radiation absorbed doses and tumor-to-normal-tissue radiation ratios. It is concluded that liposome-mediated radionuclide tumor targeting for radiotherapy is certainly promising, and critically dependent on the optimal matching between radionuclide half-life and the time range when the tumor-to-(critical)organ liposome accumulation ratios become maximal. Liposome-mediated chemotherapy (drug targeting) is also comparatively discussed demonstrating the predominant importance of 'timing factors' in the case of radiotherapeutic (radionuclide targeting) applications.

L16 ANSWER 65 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1999:593365 Document No. 132:88885 Efficient liposome-mediated gene transfer to rabbit carotid arteries in vivo. Keogh, Michael-Christopher; Chen, Daxin (Department of Immunology, Imperial College School of Medicine, London, UK). Methods in Molecular Medicine, 30(Vascular Disease: Molecular Biology and Gene Therapy Protocols), 385-394 (English) 1999. CODEN: MMMEFN. Publisher: Humana Press Inc..
AB Presented is a protocol using the com. available cationic liposome Tfx®-50 for in vivo gene delivery to rabbit carotid arteries. Procedures are described for the introduction of liposome-plasmid **conjugates** and immunohistochem. detection of cloned protein. The transfection conditions described here are optimized for gene delivery to rabbit vascular smooth muscle cells.

L16 ANSWER 66 OF 179 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
2000:317360 Document No.: PREV200000317360. Preparation and experimental study on liver-targeting liposomes (LTLp). Chen Yongpeng [Reprint author]; Zhang Lian [Reprint author]; Lu Qiaosheng [Reprint author]; Luo Kangxian [Reprint author]. Department of Infectious Diseases, Nanfang Hospital, Guangzhou, China. Journal of Gastroenterology and Hepatology, (Dec., 1999) Vol. 14, No. Suppl. A, pp. A363. print.
Meeting Info.: Second International Symposium on Hepatology. Beiging, China. December 05-09, 1999.
CODEN: JGHEEO. ISSN: 0815-9319. Language: English.

L16 ANSWER 67 OF 179 MEDLINE on STN DUPLICATE 20
2000075364. PubMed ID: 10592465. Antigen-specific, IgE-selective

unresponsiveness induced by antigen-**liposome conjugates**
. Comparison of four different conjugation methods for the coupling of antigen to liposome. Nakano Y; Mori M; Nishinohara S; Takita Y; Naito S; Horino A; Kato H; Taneichi M; Ami Y; Suzaki Y; Komuro K; Uchida T. (NOF Corp., Tsukuba Research Laboratory, Ibaraki, Japan.) International archives of allergy and immunology, (1999 Nov) 120 (3) 199-208. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB BACKGROUND: We have previously reported that ovalbumin (OVA) coupled with liposome via glutaraldehyde (GA) induced OVA-specific- and IgE-selective unresponsiveness in mice. METHODS: In this study, OVA-**liposome conjugates** were made using four different coupling protocols: via GA, N-(6-maleimidocaproyloxy) succinimide (EMCS), disuccinimidyl suberate (DSS) and N-succimidyl-3(2-pyridyldithio)propionate (SPDP) and the induction of antigen-specific IgG and IgE antibody production was investigated for each. In addition, antigen-specific cytokine production by spleen cells of mice immunized either with OVA-liposome or with OVA adsorbed with aluminum hydroxide was investigated. RESULTS: OVA-**liposome conjugates** coupled via GA or DSS did not induce anti-OVA IgE antibody production but induced substantial anti-OVA IgG antibody production. On the other hand, the induction of anti-OVA IgE unresponsiveness by OVA-**liposome conjugates** coupled via EMCS or SPDP was incomplete. The amount of interleukin 4 (IL-4) produced by spleen cells stimulated in vitro with OVA correlated well with anti-OVA IgE antibody production in donor mice. However, the production of no other cytokine, i.e., IL-2, IL-5, IL-10 or interferon-gamma, was correlated with in vivo IgE antibody production. CONCLUSION: OVA-liposome coupled via GA or DSS induced complete suppression of anti-OVA IgE production. The results in this study further suggest that the regulation of IgE antibody production does not necessarily correlate with so-called Th1 cytokine production.

L16 ANSWER 68 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2000:855864 Document No. 135:126974 Target therapy, gene therapy and DDS. Mayumi, Tadanori; Igarashi, Rie (Graduate School of Pharmacology, Osaka University, Japan). Iwanami Koza Gendai Igaku no Kiso, Volume 13, 191-215. Editor(s): Kato, Ryuichi; Mizushima, Yutaka. Iwanami Shoten: Tokyo, Japan. (Japanese) 1999. CODEN: 69APDH.

AB A review with 14 refs. on drug targeting system, covering lipid microsphere, **liposome**, **conjugates**, component vaccine, etc. The drug targeting for gene therapy including development of non-viral vectors, and future drug delivery systems are also disclosed.

L16 ANSWER 69 OF 179 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 21
1999244158 EMBASE Lectins: Sources, activities, and applications. Singh R.S.; Tiwary A.K.; Kennedy J.F.. J.F. Kennedy, Research Laboratory, School of Chemistry, University of Birmingham, Birmingham B15 2TT, United Kingdom. Critical Reviews in Biotechnology 19/2 (145-178) 1999.
Refs: 266.
ISSN: 0738-8551. CODEN: CRBTE5. Pub. Country: United States. Language: English. Summary Language: English.

AB Lectins are glycoproteins or oligomeric proteins with one or more sugar-binding site(s) per subunit. These molecules are of nonimmune origin and bind reversibly with specific sugars and precipitate polysaccharides, glycoproteins, and glycolipids bearing specific sugars, thus acting as cell recognizers. They play a key role during the initiation of infections in the altered behavior of cells during metastasis and in protection of neonates against environmental antigens. The specificity of lectins for certain sugars has been used as probes to detect cell surface sugars, enzymes, immunoglobulins, and to identify tumorogenic cells. Lectin-**liposome conjugates** have also found applications for targeted drug delivery. In addition, they have been used for flocculation of bacterial suspensions in the industry. This review discusses various sources of lectins and the mechanism behind their potential role in

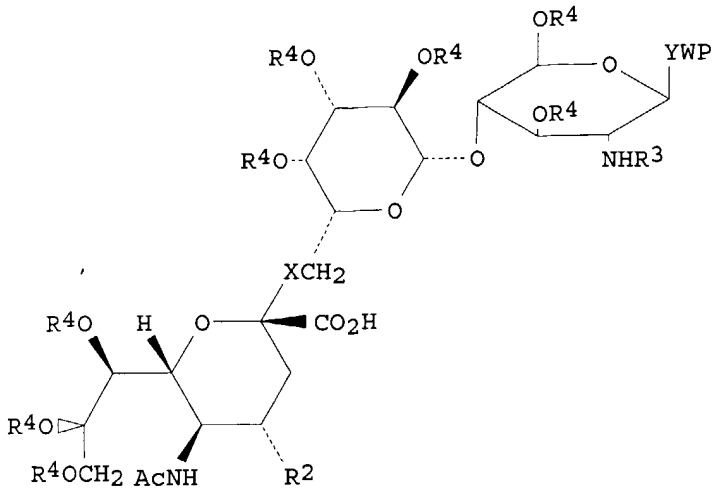
diverse fields of biological interest.

L16 ANSWER 70 OF 179 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
1999:736069 The Genuine Article (R) Number: 225QX. Cytokine production by CD4(+) T cells of mice immunised with antigen-**liposome conjugates**.. Horino A (Reprint); Naito S; Taneichi M; Kato H; Komuro K; Uchida T. NATL INST INFECT DIS, TOKYO 2080011, JAPAN. JOURNAL OF LEUKOCYTE BIOLOGY (JUN 1999) Supp. [S], pp. 55-55. Publisher: FEDERATION AMER SOC EXP BIOL. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998. ISSN: 0741-5400. Pub. country: JAPAN. Language: English.

L16 ANSWER 71 OF 179 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
1999:408928 Document No.: PREV199900408928. Cytokine production by CD4+ T cells of mice immunized with antigen-**liposome conjugates**. Horino, A. [Reprint author]; Naito, S. [Reprint author]; Taneichi, M. [Reprint author]; Kato, H. [Reprint author]; Komuro, K. [Reprint author]; Uchida, T. [Reprint author]. National Institute of Infectious Diseases, Tokyo, 208-0011, Japan. Journal of Leukocyte Biology, (1999) No. SUPPL., pp. 18. print.
Meeting Info.: 15th International Congress of the Society for Leukocyte Biology with the European Macrophage Study Group. Cambridge, England, UK. September 22-26, 1999.
CODEN: JLBIE7. ISSN: 0741-5400. Language: English.

L16 ANSWER 72 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1999:506546 Document No. 132:73304 Sterically stabilized anti-GM3, anti-Lex immunoliposomes: targeting to B16BL6, HRT-18 cancer cells. Nam, Sang Min; Kim, Hong Sung; Ahn, Woong Shick; Park, Yong Serk (Department of Medical Technology, Yonsei University, Wonju, 220-710, S. Korea). Oncology Research, 11(1), 9-16 (English) 1999. CODEN: ONREE8. ISSN: 0965-0407. Publisher: Cognizant Communication Corp..
AB Various tumor-associated antigens have been identified as carbohydrates bound to lipids or to proteins expressed on tumor cell membranes. We prepared tumor-specific immunoliposomes by coupling anticarbohydrate antibodies, such as antiganglioside GM3 antibody (DH2) or anti-Lex antibody (SHI), to polyethylene glycol (PEG)-coated liposomes. In vitro and in vivo targetability of anti-GM3 and anti-Lex immunoliposomes to B16BL6 mouse melanoma cells and HRT-18 human colorectal adenocarcinoma cells were monitored with a fluorescence microscopy, and analyzed by biodistribution assay of the immunoliposome in mice bearing the tumor tissues. The antibody coupling to the PEG liposomes did not greatly diminish the circulation time of the liposome in the C57BL/6 mouse model. In vitro cytotoxicity of doxorubicin encapsulated in liposomes was enhanced by antibody coupling, but still behind free doxorubicin. However, in vivo antitumor therapeutic efficacy of doxorubicin encapsulated in the immunoliposomes was far greater than the free drug or in conventional liposomes. Doxorubicin encapsulated in anti-GM3 immunoliposomes was able to reduce in vivo tumor growth and metastasis of B16BL6 mouse melanoma cells more greatly than any other formulations of the drug. This study suggests that tumor-associated antigens can be good target mols. for tumor-specific delivery of liposomal drugs or other synthetic drug delivery systems.

L16 ANSWER 73 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1998:219739 Document No. 128:278972 Glycoconjugates as virus cell adhesion inhibitors. Bovin, Nikolai; Matrosovich, Mikhail; Tuzikov, Alexandr; Chinarev, Alexandr; Gambaryan, Alexandra; Robertson, James (Syntesome Gesellschaft fuer Med. Biochemie m.b.H., Germany). PCT Int. Appl. WO 9814215 A2 19980409, 20 pp. DESIGNATED STATES: W: CA, JP, US; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (German). CODEN: PIXXD2. APPLICATION: WO 1997-EP5389 19971001. PRIORITY: DE 1996-19640791 19961002.
GI



I

AB The host-cell adhesion by human influenza viruses is inhibited by 6'-sialyl-N-acetyllactosamine **conjugates** [I; R1, R3 = acyl, thioacyl; R2 = H, OH, ZA; A = (substituted) alkyl, (substituted) aryl; Z = O, S, NH; R4 = H, acyl; X = O, S, C1-4 alkylene; W = bifunctional spacer; P = multivalent carrier [polyacrylate, (N-substituted) polyacrylamide, (N-substituted) methacrylamide, poly(acrylic acid), polycarbonate, polyester, polyamide, polyanhydride, polyiminocarbonate, poly(ortho ester), polydioxanone, polyphosphazene, poly(hydroxy carboxylic acid), poly(amino acid), polysaccharide, protein, dextran, chitosan, glucan, liposomes, microparticles]]. I can bind to human influenza A (H1 and H3) and B viruses which have not been adapted by culturing in chicken eggs and therefore have an unaltered structure of the receptor-binding site on the viral hemagglutinin; they are useful prophylactically and therapeutically against influenza virus infections. Thus, 6'-sialyl-N-acetyllactosamine ammonium salt was converted to its N-glycyl derivative (II) by reaction with chloroacetic anhydride. Poly(4-nitrophenyl acrylate) was 20% substituted with II by reaction with II and ethanolamine to form II-substituted poly[N-(2-hydroxyethyl)acrylamide]. The affinity constant of this polymer **conjugate** for all strains of influenza A and B virus tested was in the range 0.01-0.1 μM, as determined by its inhibition of viral binding to fetuin.

L16 ANSWER 74 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1998:534822 Document No. 129:133385 Liposome-enhanced immunoassay and test device. Durst, Richard Allen; Reeves, Stuart Graham; Siebert, Sui Ti Atienza (Cornell Research Foundation, Inc., USA). U.S. US 5789154 A 19980804, 23 pp. (English). CODEN: USXXAM. APPLICATION: US 1993-135741 19931012.

AB A test device is described for detecting or determining an analyte in a test solution and includes an absorbent material having sep. contact, competitive binding, and measurement portions. The contact portion is positioned for contact with and uptake of the test solution The competitive binding portion has a binding material for the analyte non-diffusively bound thereto. The measurement portion has a receptor for the analyte and marker-encapsulating liposomes non-diffusively bound thereto. In a method for using the test device, a solution containing the analyte and the analyte-**liposome conjugate** is allowed to traverse the absorbent material from the contact portion through the competitive binding portion and on through the measurement portion of the absorbent material. The amount of marker in the measurement portion of the absorbent material, following traversal by the test solution, is then determined as a measure of the analyte in the sample.

L16 ANSWER 75 OF 179 MEDLINE on STN DUPLICATE 22

1998214912. PubMed ID: 9554291. Ovalbumin coupled either with murine red blood cells or liposome induces IgG but not IgE antibody production. Uchida T; Naito S; Horino A; Taneichi M; Mizuguchi J; Nakano Y; Oka T; Ookuma K; Morokuma K; Sakurai S; Komuro K. (Dept. of Safety Research on Biologics, National Inst. of Infectious Diseases, Tokyo, Japan.) Developments in biological standardization, (1998) 92 353-63. Journal code: 0427140. ISSN: 0301-5149. Pub. country: Switzerland. Language: English.

AB Ovalbumin (OVA) was coupled with murine red blood cells (MRBC) using glutaraldehyde. The OVA-MRBC **conjugate** induced anti-OVA IgG antibody in mice at almost the same level as OVA in alum. However, no IgE antibody production specific for OVA was observed in OVA-MRBC-injected mice. A significant increase in IGG2a production was obtained with OVA-MRBC immunization, whereas the production of IgG1 predominated in OVA in alum immunization. Am OVA-**liposome conjugate** induced IgE-specific unresponsiveness in mice in the same manner as OVA-MRBC. Similar results were obtained when antigens other than OVA, such as tetanus toxoid or diphtheria toxoid, were coupled to liposome. These results show the potential of antigen-**liposome conjugates** for the development of vaccine that induces sufficient IgG antibody production without IgE synthesis.

L16 ANSWER 76 OF 179 MEDLINE on STN DUPLICATE 23

1998359879. PubMed ID: 9693282. Induction of protection against oral infection with cytotoxin-producing Escherichia coli O157:H7 in mice by shiga-like toxin-**liposome conjugate.** Fukuda T; Kimiya T; Takahashi M; Arakawa Y; Ami Y; Suzaki Y; Naito S; Horino A; Nagata N; Satoh S; Gondaira F; Sugiyama J; Nakano Y; Mori M; Nishinohara S; Komuro K; Uchida T. (Department of Bacterial and Blood Products, National Institute of Infectious Diseases, Tokyo, Japan.) International archives of allergy and immunology, (1998 Aug) 116 (4) 313-7. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB We have previously reported that purified Shiga-like toxins (SLT), SLT-I and SLT-II coupled with liposomes induced a substantial amount of anti-SLT-I and anti-SLT-II IgG antibody production, respectively, in mice. The levels of anti-SLT antibody in the sera of SLT-liposome-immune mice correlated well with the protection against subsequent challenge with SLT. In this study, mice were immunized intraperitoneally with the mixture of SLT-I-liposome and SLT-II-liposome and protection against oral infection with cytotoxin-producing Escherichia coli O157:H7 was evaluated. All of the mice that received immunization with the mixture of SLT-I-liposome and SLT-II-liposome were protected against subsequent intravenous challenge with 10 LD50 of either SLT-I or SLT-II. Eight weeks after primary immunization, mice were inoculated intragastrically with 10(9) CFU of E. coli O157:H7 strain 96-60. All SLT-liposome-immune mice tested survived without any apparent symptom while control mice died within 5 days. In addition, as shown by other antigen-**liposome conjugates**, SLT-liposome induced undetectable anti-SLT IgE antibody production while they induced substantial amounts of anti-SLT IgG antibodies. These results suggest that SLT-**liposome conjugate** may serve as a candidate vaccine that induces protection against cytotoxin-producing E. coli infection.

L16 ANSWER 77 OF 179 MEDLINE on STN DUPLICATE 24

1998359224. PubMed ID: 9693269. Induction of protection against tetanus toxin in mice by tetanus toxoid-**liposome conjugate.** Naito S; Horino A; Komiya T; Fukuda T; Takahashi M; Ami Y; Suzaki Y; Oka T; Okuma K; Morokuma M; Nakano Y; Mori M; Nishinohara S; Komuro K; Uchida T. (Department of Safety Research on Biologics, National Institute of Infectious Diseases, Tokyo, Japan.) International archives of allergy and immunology, (1998 Jul) 116 (3) 215-9. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB Tetanus toxoid (Ttd) was coupled to liposomes via glutaraldehyde. Intraperitoneal injection in BALB/c mice with Ttd-liposomes induced a substantial amount of anti-Ttd IgG antibody production and an extremely

low level of anti-Ttd IgE antibody production. Mice immunized with Ttd-liposomes were successfully protected against a subsequent challenge with a lethal dose of tetanus toxin (Ttx). On the other hand, aluminum hydroxide-adsorbed Ttd (Ttd-alum) and plain Ttd solution induced the production of both IgG and IgE antibodies against Ttd. Moreover, secondary immunization with Ttd-liposomes in mice, in which anti-Ttd IgE antibody production was induced by Ttd-alum led to enhanced anti-Ttd IgG and a limited anti-Ttd IgE antibody production. When Ttd-liposome preparation was lyophilized, the efficacy of Ttd-liposomes was maintained for 6 months at 37 C, suggesting that this vaccine preparation would be stable without refrigeration. These results demonstrate the potential ability of Ttd-**liposome conjugates** to produce a tetanus vaccine which provides protection against (Ttx) while inducing the least amount of anti-Ttd IgE antibodies.

L16 ANSWER 78 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1998:790795 Document No. 130:193757 Preparation of neoglycoprotein-**liposome conjugates** and their applications for studying recognition functions based on membrane-surface carbohydrate-protein interactions. Yamazaki, Noboru (Dep. Org. Mater., Natl. Inst. Mater. Chem. Res., Tsukuba, 305-8565, Japan). Busshitsu Kogaku Kogyo Gijutsu Kenkyusho Hokoku, 6(5), 199-211 (English) 1998. CODEN: BKGHE2. ISSN: 0919-7087. Publisher: Busshitsu Kogaku Kogyo Gijutsu Kenkyusho.
AB A review with 42 refs. In order to find a route from biol. phenomena to possible applications in the organic materials science, the authors have paid special attention to carbohydrate-protein interactions which play an important role in biol. systems. Studies on these interactions are attracting increasing interests in synthetic research and in practical applications in various fields for producing new functional materials. The authors discuss the preparation and characterization of neoglycoprotein-**liposome conjugates**, and applications for studying recognition functions of these neoglycoconjugates using a model system and biol. systems. Various types of neoglycoprotein-**liposome conjugates** have been prepared according to a method, including preparation of mixed micelles, preparation of liposomes, and chemical coupling of neoglycoproteins to liposomes. A model study and in vitro assays using human adenocarcinoma cells indicates carbohydrate-specific recognition functions of these neoglycoprotein-**liposome conjugates**. A tissue distribution assay using Ehrlich solid tumor-bearing mice shows individual response of diverse tissues toward different types of applied neoglycoprotein-**liposome conjugates.** This new type of carbohydrate-conjugated materials will find a wide field of applications for basic carbohydrate recognition research as well as for applied areas such as cell type-specific targeting materials.

L16 ANSWER 79 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
2001:861063 Document No. 136:228571 Fetuin-**liposome conjugates** and immobilized lectins as a model system for studying multivalent carbohydrate-lectin interactions. Yamazaki, N.; Kaihou, S.; Shoda, M.; Ito, Y.; Sakuta, H.; Katsura, T.; Mizutani, F. (National Institute of Materials and Chemical Research, Tsukuba Science City, Japan). Lectins: Biology, Biochemistry, Clinical Biochemistry [online computer file], 12, No pp. given (English) 1998. CODEN: LBBBD5. ISSN: 0723-8878. URL: http://plab.ku/dk/tcbh/Lectins12/Yamazaki/paper.htm Publisher: Lectins: Biology, Biochemistry, Clinical Biochemistry.
AB The preparation and binding properties of new types of liposomal systems, such as bovine fetuin-bearing liposomes, were reported. Results showed that among a series of fetuin-**liposome conjugates**, the increase in sialic acid d. on the liposome surface significantly enhances the binding potency of liposomal neoglycoconjugates. Sugar chains on fetuin proteins, which are covalently conjugated on the surface of bimol. lipid membrane of liposomes, showed higher binding affinity than the uncoupled natural fetuins. The interaction of a series of sialidase-treated fetuin-**liposome conjugates** with

Maackia amurensis lectin (MAL) was proportional to the sialic acid d. on the liposomal surface, while the interaction with Sambucus sieboldiana lectin did not appear to show the similar dependence.

L16 ANSWER 80 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1998:42419 Document No. 128:110866 Recombinant ribosomal inhibitor protein (RIP) and its use as an antitumor immunoconjugate. Mele, Antonio; De Santis, Rita; Parente, Dino; Colnaghi, Maria Ines (Ministero Universita' Ricerca Scientifica e Tecnologica, Italy; Mele, Antonio; De Santis, Rita; Parente, Dino; Colnaghi, Maria Ines). PCT Int. Appl. WO 9749726 A1 19971231, 25 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-EP3359 19970626. PRIORITY: IT 1996-FI155 19960627.
AB The following description refers to a new RIP protein, the cDNA sequence encoding it, its preparation and use in the preparation of chemical and recombinant **conjugates** having anticancer properties.

L16 ANSWER 81 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1997:745956 Document No. 128:30403 Bismuth salts of sialyloligosaccharides and a method for treating and inhibiting gastric and duodenal ulcers using them. Swarz, Herbert (Neose Technologies, Inc., USA). PCT Int. Appl. WO 9741875 A1 19971113, 41 pp. DESIGNATED STATES: W: AU, CA, JP, KR, MX; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US6376 19970428. PRIORITY: US 1996-16765 19960503.
AB A method for treating and/or inhibiting gastric and duodenal ulcers comprises administering a pharmaceutical composition comprising a bismuth salt of an oligosaccharide (NeuAc-α(2-3)-pGal-β(1)-(X)m-(Y)n-)p-Z, (X = bond or group capable of linking pGal to either linking group Y or multivalent support Z; C1 glycosidic O of galactose may be replaced by N, S, C; Y = linking group; Z = multivalent support; m, n = 0, 1; p = 2-1000) is described. Also described is a method for treating and/or inhibiting gastric and duodenal ulcers, comprising administering a pharmaceutical composition comprising a bismuth salt of an oligosaccharide NeuAc-α(2-3)-pGal-β(1)-A (A = group capable of bonding to pGal; C1 glycosidic O of galactose may be replaced by N, S, C).

L16 ANSWER 82 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1997:517559 Document No. 127:156736 Growth hormone peptide **conjugates** having growth hormone-potentiating activity and their use in food additives to stimulate growth and lactation. Portetelle, Daniel; Renaville, Robert (Carelli, Claude Marcel Henri, Fr.; Hebert, Etienne Francois Marcel). PCT Int. Appl. WO 9727298 A1 19970731, 25 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (French). CODEN: PIXXD2. APPLICATION: WO 1997-FR127 19970122. PRIORITY: FR 1996-956 19960126.
AB A peptide construct including all or part of the sequence between positions 104 and 113 of growth hormone GH, or a homologous sequence cross-reactive therewith, is disclosed. The peptide fragment is covalently bonded to a transporter peptide and/or an adjuvant, and is capable of having an in vivo potentiating effect on the biol. activity of said growth hormone. The GH-potentiating effect of GH peptides conjugated to ovalbumin and syncytial respiratory virus protein 1A peptides was demonstrated in hypophysectomized rats.

L16 ANSWER 83 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1997:207654 Document No. 126:199966 Manufacture of polyethylene glycol (PEG) monosubstituted with carboxyethyl- or carboxypropyl groups and their functional derivatives for biotechnical applications. Harris, J. Milton; Kozlowski, Antoni (Shearwater Polymers, Inc., USA; Harris, J. Milton; Kozlowski, Antoni). PCT Int. Appl. WO 9703106 A1 19970130, 39 pp. DESIGNATED STATES: W: AL, AM, AT, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US11261 19960703. PRIORITY: US 1995-499321 19950707; US 1995-642231 19951002.

AB Active esters of PEG-acids and related polymers are provided that have a single propionic or butanoic acid moiety and no other ester linkages. These esters have a half life in H2O of 10-25 min. For example, α-methoxy, ω-propionic acid succinimidyl ester of PEG ("methoxy-PEG-SPA") has a nearly ideal reactivity with NH2 groups on proteins and other biol. active substances. The half life of methoxy-PEG-SPA is .apprx.16.5 min in H2O. The invention also provides **conjugates** with proteins, enzymes, polypeptides, drugs, dyes, nucleosides, oligonucleotides, lipids, phospholipids, liposomes, and surfaces of solid materials that are compatible with living organisms, tissue, or fluid. For example, polyethylene glycol monomesylate was heated for 3 h under N with HSCH2CH2CO2Et in a EtOH/PhMe mixture containing NaOH and the product saponified with aqueous NaOH at room temperature to give HO(CH2CH2)nCH2CH2SCH2CH2CO2H. This was esterified with acryloyl chloride in CH2Cl2 in the presence of Et3N, the monoester esterified with N-hydroxysuccinimide in CH2Cl2 in the presence of N,N'-dicyclohexylcarbodiimide and the resulting active ester coupled with subtilisin.

L16 ANSWER 84 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1997:656845 Document No. 127:293805 Preparation of poly(ethylene glycol) monosubstituted with propionic or butanoic acids and functional derivatives thereof for biotechnical applications. Harris, J. Milton; Kozlowski, Antoni (Shearwater Polymers, Inc., USA). U.S. US 5672662 A 19970930, 11 pp., Cont.-in-part of U.S. Ser. No. 499,321, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1995-642231 19951002. PRIORITY: US 1995-499321 19950707.

AB Title polymers, useful to **conjugate** with proteins, enzymes, polypeptides, drugs, dyes, nucleosides, oligonucleotides, lipids, phospholipids, liposomes, and surfaces of solid materials that are compatible with living organisms, tissue, or fluid, contain a single propionic or butanoic acid moiety and have a half life in water of from about 10 to 25 min. Thus, α-methoxy-ω-propionic acid succinimidyl ester of polyethylene glycol (CH3O-PEG-SPA) was prepared by reaction of methoxy-PEG and acetonitrile, hydrolysis with hydrochloric acid to form amide and then with potassium hydroxide to form acid, followed by reaction with N-hydroxysuccinimide, showing half life about 16.5 min in water and a nearly ideal reactivity with amino groups on proteins and other biol. active substances.

L16 ANSWER 85 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1997:148830 Document No. 126:176898 antigen-linked liposomes as vaccines. Nakano, Yoshiro; Uchida, Tetsuya (Nippon Oils & Fats Co Ltd, Japan; Kokuritsu Yobo Eisei Kenkyusho). Jpn. Kokai Tokkyo Koho JP 09012480 A2 19970114 Heisei, 8 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1995-166444 19950630.

AB Antigens are linked to amino group-containing liposomes (1-3μm) to form antigen-**liposome conjugate**-type vaccines.

L16 ANSWER 86 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1997:506897 Document No. 127:166773 **Conjugates** of lipids and

membrane-disturbing peptides as transfection-competent molecules. Legendre, Jean-Yves; Supersaxo, Andreas; Trzeciak, Arnold (F. Hoffmann-La Roche Ag, Switz.). Eur. Pat. Appl. EP 784984 A2 19970723, 11 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1997-100208 19970109. PRIORITY: EP 1996-100603 19960117.

AB The invention relates to **conjugates** of lipids and basic, membrane disturbing peptides, particularly, compds. of the formulas (R-CONH)n-R3 and (R-S-S)n-R3 (wherein R is the hydrocarbyl moiety of a straight-chain or branched-chain, saturated or unsatd. aliphatic carboxylic acid, or a phospholipid moiety having a free valence bond; R3 is a basic membrane disturbing peptide having a free valence bond at one or two carbon atom(s); and n is 1 or 2). These can be used as a vector for transfecting a cell with a polynucleotide or any other anionic macromol.

L16 ANSWER 87 OF 179 MEDLINE on STN DUPLICATE 25

1998028542. PubMed ID: 9363912. Protection against verocytotoxin in mice induced by liposome-coupled verocytotoxin. Naito S; Horino A; Komiya T; Fukuda Y; Takahashi M; Ami Y; Suzaki Y; Satoh S; Gondaira F; Sugiyama J; Nakano Y; Mori M; Awai K; Nishinohara S; Komuro K; Uchida T. (Department of Safety Research on Biologics, National Institute of Infectious Diseases, Musashimurayama, Tokyo, Japan.) International archives of allergy and immunology, (1997 Nov) 114 (3) 293-7. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB Purified verocytotoxins (VTs), VT1 and VT2, were coupled to liposomes via glutaraldehyde. During the coupling procedure, both VT1 and VT2 were detoxified. Intraperitoneal injection in BALB/c mice with either VT1-liposome or VT2-liposome induced a substantial amount of anti-VT1 or anti-VT2 IgG antibody production, respectively. Mice immunized with VT2-liposome were protected against intravenous challenge with a lethal dose of VT2 and the degree of protection correlated well with the amount of IgG induced against VT2. Although VT1-liposome failed to induce protection against VT1, the decrease of the body weight observed after the toxin challenge correlated inversely with the amount of anti-VT1 IgG induced, suggesting that VT1 neutralizing antibody was present in VT1-liposome-immune mice. In addition, VT-**liposome conjugate** induced no detectable anti-VT IgE antibody production. These results demonstrate the potential ability of VT-**liposome conjugates** for the production of VT vaccine which induces protection against VTs.

L16 ANSWER 88 OF 179 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 26

1998:48344 Document No.: PREV199800048344. Cytokine production by spleen cells from mice with ovalbumin-specific, IgE-selective unresponsiveness induced by ovalbumin-**liposome conjugate.** Horino, Atsuko; Taneichi, Maiko; Naito, Seishiro; Ami, Yasushi; Suzaki, Yuriko; Komuro, Katsutoshi; Uchida, Tetsuya [Reprint author]. Dep. Safety Res. on Biologics, Natl. Inst. Infectious Diseases, 4-7-1 Gakuen, Musashimurayama, Tokyo 208, Japan. Allergology International, (Dec., 1997) Vol. 46, No. 4, pp. 249-253. print.
ISSN: 1323-8930. Language: English.

AB Ovalbumin coupled with liposomes (OVA-liposome) induced selective unresponsiveness of anti-OVA IgE antibody production in BALB/c mice, whereas OVA adsorbed with aluminum hydroxide (OVA-alum) induced a substantial amount of anti-OVA IgE antibody production. Ovalbumin-liposome and OVA-alum predominantly induced IgG2a and IgG1 anti-OVA production, respectively. These results suggest that OVA-liposome and OVA-alum induce type 1 and type 2 T helper (Th) immune responses, respectively. To further investigate this issue, we examined the cytokine production induced by these two distinct adjuvants. Spleen cells taken from mice immunized with either OVA-liposome or OVA-alum were cultured in vitro with OVA and the cytokine production from each culture was analyzed. It was demonstrated that spleen cells from mice immunized

with OVA-liposome produced more interferon (IFN)-gamma than those immunized with OVA-alum and, furthermore, interleukin (IL)-4 was produced only by spleen cells from mice immunized with OVA-alum. These results favor the notion that OVA-liposome and OVA-alum induce Th 1 and Th2 cytokines, respectively. Interestingly, the production of IL-2, a Th1 cytokine, was higher in the OVA-alum-immunized group and the production of IL-10, a Th2 cytokine, remained at low levels in both groups after primary immunization; levels of IL-10 increased in the OVA-liposome-immunized group after secondary immunization. These results do not agree with the above notion and, thus, suggest that it may be important to consider the balance between IFN-gamma-producing cells and IL-4-producing cells rather than that between Th1 and Th2 cells for the regulation of IgE antibody production.

L16 ANSWER 89 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1997:568390 Document No. 127:233308 Specific inhibition of cell adhesion by exogenous glycoligands. Stahn, R.; Schreiber, J.; Schafer, H. (Max-Delbruck-Centre for Molecular Medicine, Berlin, D-13122, Germany). Lectins: Biology, Biochemistry, Clinical Biochemistry, 11, 193-197 (English) 1997. CODEN: LBBBD5. ISSN: 0723-8878. Publisher: TEXTOP.
AB The inhibition of KG-1 leukemia cell (expressing the Thomsen-Friedenreich (TF) antigen) adhesion, to galactose-specific receptors by different cluster galactosides is reported. Different galactose-specific lectins located on HepG2 hepatoma cells or immobilized on plastic wells (Ricinus communis lectin) were tested with respect to the adhesion of leukemia cells in the presence of galactosides. Of the galactosides tested, the asialofetuin was most powerful in inhibiting cell adhesion. Glycoliposomes are also very potent inhibitors. Thus, the multiple presentation of terminal β-galactose-residues by cluster glycosides enhances the inhibition of adhesion of KG-1 cells, expressing the TF-antigen, to galactose-specific receptors immobilized on plastic wells or located on cell surfaces.

L16 ANSWER 90 OF 179 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
97:819052 The Genuine Article (R) Number: YA741. Fetuin-**liposome conjugates** and immobilized lectins as a model system for studying multivalent lectin-carbohydrate interactions. Yamazaki N (Reprint); Kaihou S; Sakuta H; Katsura T; Mizutani F. NATL INST MAT & CHEM RES, TSUKUBA, IBARAKI 305, JAPAN; NATL INST BIOSCI & HUMAN TECHNOL, TSUKUBA, IBARAKI 305, JAPAN. EUROPEAN JOURNAL OF CELL BIOLOGY (NOV 1997) Vol. 74, Supp. [46], pp. 115-115. Publisher: WISSENSCHAFTLICHE VERLAG MBH. BIRKENWALDSTRASSE 44, POSTFACH 10 10 61, 70009 STUTTGART, GERMANY. ISSN: 0171-9335. Pub. country: JAPAN. Language: English.

L16 ANSWER 91 OF 179 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
1998:66302 Document No.: PREV199800066302. Fetuin-**liposome conjugates** and immobilized lectins as a model system for studying multivalent lectin-carbohydrate interactions. Yamazaki, Noboru [Reprint author]; Kaihou, Shinobu [Reprint author]; Sakuta, Hiroko [Reprint author]; Katsua, Tatsuo; Mizutani, Fumio. Natl. Inst. Mater. Chem. Res., Higashi 1-1, Tsukuba, Ibaraki 305, Japan. European Journal of Cell Biology, (1997) Vol. 74, No. SUPPL. 46, pp. 39. print.
Meeting Info.: 7th International Lectin Meeting. Wuerzburg, Germany. September 24-27, 1997.
CODEN: EJCBDN. ISSN: 0171-9335. Language: English.

L16 ANSWER 92 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1996:761876 Document No. 126:37102 Compositions and methods useful for inhibiting cell death and for delivering an agent into a cell. Khaw, Ban An; Torchilin, Vladmir P.; Narula, Jagat; Vural, Imran (Northeastern University, USA). PCT Int. Appl. WO 9633698 A1 19961031, 60 pp. DESIGNATED STATES: W: AU, JP; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US5181 19960416. PRIORITY: US 1995-427676 19950424.
AB The invention relates to methods of salvaging a target cell from cell

death, comprising contacting a target cell having a disrupted cell membrane with a specific affinity reagent-**liposome conjugate** in an amount effective and for a time sufficient to allow the **conjugate** to prevent cell death due to membrane disruption; and determining the viability of the target cell. Methods of delivering a selected agent into a damaged target cell for diagnosis and therapy are also disclosed.

L16 ANSWER 93 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1996:446972 Document No. 125:96049 Method and compositions containing human bile salt lipase fragment for reducing intestinal absorption of cholesterol. Tang, Jordan J. N.; Wang, Chi-Sun (Oklahoma Medical Research Foundation, USA). PCT Int. Appl. WO 9617054 A1 19960606, 99 pp. DESIGNATED STATES: W: AU, CA, JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US15647 19951201. PRIORITY: US 1994-347718 19941201; US 1995-479160 19950607; US 1995-482262 19950607.

AB Compns. derived from all or a portion of the carboxy terminal region of human bile salt-activated lipase (BAL) are described, which, when orally ingested, compete with native BAL in binding to the intestinal surface, thus reducing the physiol. role of BAL in mediating the transfer of cholesterol into the intestinal cells, and, as a result, reducing the amount of cholesterol absorbed from the intestine into the blood stream. Useful derivs. of the carboxy terminal region of BAL are derived from all or portion of the region containing amino acid residues 539 to 722, and have a mucin-like structure containing at least three of the repeating proline-rich units of eleven amino acid residues each. **Conjugates** of the BAL peptide and biol. active substances (such as proteins, vitamins, chemotherapeutic agents, etc.) are also claimed. The C-terminus of BAL was found to be involved in binding of BAL to intestinal epithelial lining cells. Addition of the C-terminal fragment to intestinal content released bound endogenous BAL. This fragment competitively inhibited cholesterol uptake in the rat intestine. BAL was shown to mediate uptake of triglycerides but not taurocholate in isolated rat intestinal tissue.

L16 ANSWER 94 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1996:425347 Document No. 125:67771 Glycosylated protein-**liposome conjugates** and methods for their preparation. Ansell, Steven Michial (Inex Pharmaceuticals, Inc., Can.). PCT Int. Appl. WO 9610585 A1 19960411, 41 pp. DESIGNATED STATES: W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-CA554 19950929. PRIORITY: US 1994-316394 19940930; US 1995-418696 19950407.

AB The present invention provides glycosylated protein-liposome compns. which are useful for the targeted delivery of a therapeutic agent. The compns. comprise an oxidized protein, typically an antibody, which is covalently attached to a lipid by means of a crosslinking agent having an acid hydrazide functionality on one terminus and a sulfhydryl functionality on the other terminus. The lipid is present in a liposome formulation. Methods for preparing the compns. are also provided. In the methods, a glycosylated protein is first oxidized then reacted with a linking group having an acid hydrazide on one end and a sulfhydryl or protected sulfhydryl group on the other end. The resultant modified protein is then reacted with a liposome formulation of a lipid having a sulfhydryl reactive functional group to covalently attach the protein to the liposome.

L16 ANSWER 95 OF 179 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
1996:343581 Document No.: PREV199699065937. Bioconjugate techniques. Hermanson, Greg T.. Pierce Chem. Co., Rockford, IL, USA. Hermanson, G. T. (1996) pp. xxvii+785p. Bioconjugate techniques. Publisher: Academic Press, Inc., 1250 Sixth Ave., San Diego, California 92101, USA; Academic Press

Ltd., 14 Belgrave Square, 24-28 Oval Road, London NW1 70X, England, UK. ISBN: 0-12-342336-8, 0-12-342335-X. Language: English.

AB This text is a guide to the foundation and techniques necessary to design and synthesize bioconjugates for use in research, diagnostics, and therapeutics. Seventeen chapters divided into three parts comprise the text. Topics include bioconjugate chemistry, reagent systems, and applications. Functional targets, immunotoxin **conjugate** techniques, preparation of **liposome conjugates** and derivatives, and avidin-biotin systems are discussed. Step-by-step protocols are provided. Structures, graphs, and diagrams are incorporated into the text. References are provided at the end of the text.

L16 ANSWER 96 OF 179 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
96:861513 The Genuine Article (R) Number: VT565. Neoglycoprotein liposome and fetuin-**liposome conjugates.** Yamazaki N (Reprint); Kaihou S; Sakuta H; Kojima S; Gabius H J; Katsura T. NATL INST MAT & CHEM RES, MAT DESIGN LAB, TSUKUBA, IBARAKI 305, JAPAN; UNIV TOKYO, BIOSCI RES INST, NODA, CHIBA 278, JAPAN; UNIV MUNICH, INST PHYSIOL CHEM, D-8000 MUNICH, GERMANY; NATL INST BIOSCI & HUMAN TECHNOL, TSUKUBA, IBARAKI 305, JAPAN. GLYCOBIOLOGY (OCT 1996) Vol. 6, No. 7, pp. 415-415. Publisher: OXFORD UNIV PRESS UNITED KINGDOM. WALTON ST JOURNALS DEPT, OXFORD, ENGLAND 'OX2 6DP. ISSN: 0959-6658. Pub. country: JAPAN; GERMANY. Language: English.

L16 ANSWER 97 OF 179 MEDLINE on STN DUPLICATE 27
96184212. PubMed ID: 8620090. Ovalbumin-**liposome conjugate** induces IgG but not IgE antibody production. Naito S; Horino A; Nakayama M; Nakano Y; Nagai T; Mizuguchi J; Komuro K; Uchida T. (Department of Safety Research on Biologics, National Institute of Health, Tokyo, Japan.) International archives of allergy and immunology, (1996 Mar) 109 (3) 223-8. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB Antibody response after immunization with surface-coupled ovalbumin (OVA) of liposomes was investigated in mice. OVA was coupled to the surface of liposome via amino groups using glutaraldehyde. OVA-**liposome conjugate** induced a significant anti-OVA IgG antibody production in mice. However, no IgE antibody production specific for OVA was observed. Immunization with OVA-liposome induced IgE-specific unresponsiveness even after the subsequent challenge with OVA adsorbed with with aluminium hydroxide (OVA-alum), which induces a high level of IgE antibody production. Furthermore, following the primary immunization with OVA-alum, a secondary challenge with OVA-liposome boosted anti-OVA IgG but not anti-OVA IgE antibody production. These results show the potential of the antigen-**liposome conjugate** for the development of a vaccine with the least allergic reaction and also for the application of immunotherapy.

L16 ANSWER 98 OF 179 MEDLINE on STN DUPLICATE 28
96174859. PubMed ID: 8593275. Preparation and characterization of **conjugates** of (modified) human serum albumin and liposomes: drug carriers with an intrinsic anti-HIV activity. Kamps J A; Swart P J; Morselt H W; Pauwels R; De Bethune M P; De Clercq E; Meijer D K; Scherphof G L. (Groningen Institute for Drug Studies, Department of Physiological Chemistry, Groningen University, Groningen, The Netherlands.) Biochimica et biophysica acta, (1996 Jan 31) 1278 (2) 183-90. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB Human serum albumin (HSA) derivatized with cis-aconitic anhydride (Aco-HSA) that was earlier shown to inhibit replication of human immunodeficiency virus type 1 (HIV-1), was covalently coupled to conventional liposomes, consisting of phosphatidylcholine, cholesterol and maleimido-4-(p-phenylbutyryl)phosphatidylethanolamine, using the heterobifunctional reagent N-succinimidyl-S-acetylthioacetate (SATA). The amount of HSA that could be coupled to the liposomes depended on derivatization of the HSA and ranged from 64.2 +/- microgram HSA/micromol total lipid for native HSA to 29.5 +/- 2.7 microgram HSA/micromol total lipid for HSA in which 53 of the epsilon amino groups of lysine were

derivatized with cis-aconitic anhydride (Aco53-HSA). Incorporation of 3.8 mol% of total lipid of a poly(ethylene glycol) derivative of phosphatidylethanolamine (PEG-PE) in the liposomes resulted in a lower coupling efficiency of Aco-HSA. The elimination and distribution of the liposomal **conjugates** in rats in vivo was largely dependent on the modification of the HSA coupled to the liposomes. With native HSA-liposomes, more than 70% of the **conjugate** was still found in the blood plasma 30 min after i.v. injection in rats, while at this time Aco-HSA-liposomes were completely cleared from the circulation. The rapid clearance of conventional Aco-HSA-liposomes was due to a rapid uptake into the liver and could be considerably decreased by incorporating PEG-PE in the liposomal bilayer. After 3 h 60% of Aco-HSA-PEG-**liposome conjugates** were found in the blood. In an in vitro anti-HIV-1 assay, the 50% inhibitory concentrations (IC50) for Aco39-HSA-liposomes and Aco53-HSA-liposomes expressed as protein weight, were 2.87 microgram/ml and 0.154 microgram/ml, respectively. When PEG-PE was incorporated, the Aco53-HSA-liposomes retained anti HIV-1 activity (IC50:3.13 microgram/ml). The possibility to modulate the residence time in the bloodstream of Aco-HSA-liposomes and the potent anti-HIV-1 activity of these **conjugates**, may allow the development of an intrinsically active drug carrier system. By incorporating anti HIV-1 drugs such as AZT into such liposomes a drug delivery system can be designed that might act simultaneously on the virus/cell binding by virtue of the coupled Aco-HSA and on the RNA/DNA transcription of the HIV-1 replication cycle through the nucleoside analogue.

L16 'ANSWER 99 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1996:58480 Document No. 124:200135 Receptor-mediated endocytosis of poly(acrylic acid)-conjugated liposomes by macrophages. Fujiwara, Mitsuko; Baldeschwieler, John D.; Grubbs, Robert H. (Pasadena, CA, 91125, USA). Biochimica et Biophysica Acta, 1278(1), 59-67 (English) 1996. CODEN: BBACAQ. ISSN: 0006-3002. Publisher: Elsevier.

AB The uptake characteristics of neg.-charged liposomes made by conjugation of poly(acrylic acid) (PAA) were studied with respect to cultured RAW macrophages. The PAA-conjugated liposomes were internalized and digested in an acidic compartment at a much faster rate than the unmodified phosphatidylcholine (PC) liposomes. After incubation for 18 h, an over 5-fold increase in the uptake of PC liposomes was obtained by PAA conjugation. Subsequently, part of the aqueous phase of the internalized liposomes was exocytosed. Recognition of PAA by the macrophages seems to be responsible for the enhanced uptake of PAA-conjugated liposomes. Cross-competition expts. showed that PAA-conjugated liposomes inhibited the uptake of acetylated-low d. lipoprotein (acetyl-LDL) by the macrophages and vice versa. The uptake of PAA-conjugated liposomes was also inhibited by dextran sulfate and maleylated-bovine serum albumin (maleyl-BSA), which are also known to bind to scavenger receptors. Poly(C) and BSA, which are not ligands for the scavenger receptor, competed poorly with the uptake of PAA-conjugated liposomes. Enhanced uptake of PAA-conjugated liposomes by CHO cells with low scavenger receptor expression was not observed Unexpectedly, LDL, which is not a ligand for scavenger receptor, also partially inhibited the uptake of PAA-conjugated liposomes. The interaction of PAA-conjugated liposomes with macrophages is complex, and the endocytosis of PAA-conjugated liposomes most likely involves multiple receptors and/or pathways. The data obtained suggest that the high affinity binding of PAA-conjugated liposomes to macrophages may be due to recognition of the neg. charges of PAA by cell surface receptors, including the scavenger receptor.

L16 ANSWER 100 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1996:297322 Document No. 125:7774 Immunogenicity of new heterobifunctional crosslinking reagents used in the conjugation of synthetic peptides to liposomes. Boeckler, Christophe; Frisch, Benoit; Muller, Sylviane; Schuber, Francis (Laboratoire de Chimie Bioorganique, CNRS URA 1386, Faculte de Pharmacie, 74 Route du Rhin, 67400, Illkirch, Fr.). Journal of Immunological Methods, 191(1), 1-10 (English) 1996. CODEN: JIMMBG. ISSN:

0022-1759. Publisher: Elsevier.

AB The authors have investigated the immunogenicity of six thiol-reactive heterobifunctional crosslinking reagents that permit the conjugation of cysteine carrying peptides to the surface of liposome containing monophosphoryl lipid A. Such constructs elicit an immune response against short synthetic peptides and the authors' aim was to find the least immunogenic linkers to limit potential carrier-induced epitopic suppression. For that purpose the properties of three new polyoxyethylene linkers of different lengths and thiol-reactive moieties (maleimide, bromoacetyl, dithiopyridine) were compared to known derivs. obtained by reacting the classical reagents SMPB and SPDP or N-succinimidyl bromoacetate with phosphatidylethanolamine. The least immunogenic linkers were the bromoacetate derivs. whereas those containing a maleimide group evoked a significant anti-linker immune response. In addition, using IRGERA as a model peptide, the authors found that all six liposomal constructs strongly elicited the production of anti-peptide IgG antibodies. This immune response was therefore independent of the length of the linkers (ranging between 0.3 and 1.6 nm) and of the nature of the linkage between the peptide and the thiol-reactive moieties of the cross-linkers, i.e. stable thioether or bio-reducible disulfide bonds.

L16 ANSWER 101 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

1996:97268 Document No. 124:135728 Selenium **conjugates** for the preparation of free radical pharmaceuticals. Spallholz, Julian E.; Reid, Ted W. (USA). PCT Int. Appl. WO 9531218 A1 19951123, 59 pp. DESIGNATED STATES: W: AU, CA, JP, MX, NO; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US5997 19950512. PRIORITY: US 1994-243709 19940517; US 1995-432584 19950509.

AB A method is provided for making a selenium-carrier **conjugate** by covalently attaching (i) an organic selenium compound selected from RSeH, RSeR, RSeR', RSeSeR and RSeSeR', (R, R' = aliphatic residue containing ≥1 reactive group selected from aldehyde, amino, alc., carboxylic, phosphate, sulfate, halogen or phenolic reactive groups and combinations thereof), to (ii) a carrier having a constituent capable of forming a covalent bond with said reactive groups of said selenium compound to produce a selenium-carrier **conjugate** which is capable of specific attachment to a target site. The selenium reacts with thiols at the target site to generate superoxide for localized destruction or for localized inhibition of scar tissue formation. The **conjugates** are useful for treating cancer and pathogenic infections, preventing unwanted cellular growth associated with use of implants, and prevention of unwanted scarring in surgical procedures. Preparation and testing of selenocytamine-antibody **conjugates** are described, as are attachment of selenocytamine to a cellulose-matrix device and attachment of selenocytamine to plastic. Attachment of selenocystamine to plastic results in a material that inhibits cellular growth.

L16 ANSWER 102 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

1996:25269 Document No. 124:66569 Group A streptococcal polysaccharide immunogenic compositions and methods. Blake, Milan S.; Zabriskie, John B.; Tai, Joseph Y.; Michon, Francis (Rockefeller University, USA; North American Vaccine, Inc.). PCT Int. Appl. WO 9528960 A1 19951102, 66 pp. DESIGNATED STATES: W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US4973 19950420. PRIORITY: US 1994-231229 19940421.

AB This invention provides a novel immunogenic composition and vaccine, processes for producing them and methods for immunization against infectious and disease caused by group A Streptococci. The compns. include group A streptococcal polysaccharide covalently linked to protein or liposomes to form immunogenic **conjugates.** The method of immunization for

this invention comprises administering to an individual an immunogenic amount of group A polysaccharide. The group A polysaccharide may be administered as a vaccine either on its own, conjugated to proteins or conjugated to liposomes. Addnl., the group A polysaccharides may be associated with an adjuvant. This invention is particularly useful for providing both active and passive immunogenic protection for those populations most at risk of contracting group A Streptococcal infections and disease namely adults, pregnant women and in particular infants and children.

L16 ANSWER 103 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1995:875024 Document No. 124:86585 Reactive derivatives of BAPTA used to make ion-selective chelators. Kuhn, Michael A.; Haugland, Richard P. (Molecular Probes, Inc., USA). U.S. US 5453517 A 19950926, 29 pp. (English). CODEN: USXXAM. APPLICATION: US 1992-843360 19920225.
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to fluorescent and/or reactive derivs. of 1,2-bis(2-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid (BAPTA) according to the formula I where at least one of W and X is a functional group, with or without a spacer, that terminates in an alc. or phenol, a thiol, a haloacetamide, an alkyl halide, an amine or aniline, a carboxylic acid, an anhydride, an isocyanate, an isothiocyanate, a maleimide, or an activated ester. The BAPTA-like mol. may be further substituted, one or more times, by addnl. functional groups with or without spacers or by CH3, NO2, CF3, F, Cl, Br, I, or carboxylic acid derivs. or pharmaceutically acceptable salts thereof, or by indolyl or benzofuran fluorophores. The functional groups allow for subsequent covalent attachment of one or more oxygen heterocycle fluorophores (e.g. fluorescein, coumarin, rhodamine); or polymol. assemblies (e.g. gel and resin polymers, polysaccharides, polypeptides, nucleic acids, and liposomes); or combinations thereof. Thus, e.g., coupling of 5-carboxy-2',7'-dichlorofluorescein diacetate to 5-amino BAPTA tetra-Me ester (preparation given) via the mixed anhydride method afforded the BAPTA **conjugate** linked to a green fluorescent dye (II) which exhibited Ca+2 dissociation constant Kd = 189 nM and emission quantum yield in high and low Ca+2 buffers of 0.75 and 0.06, resp. (emission increase of approx. 12-fold).

L16 ANSWER 104 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1995:902922 Document No. 123:283640 Antibodies against epitopes with homology to self antigens and methods of preparation and applications. Rajewsky, Klaus; Mueller, Werner; Roes, Juergen (Mioltenyi, Stefan, Germany). Eur. Pat. Appl. EP 677533 A2 19951018, 16 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1995-302440 19950412. PRIORITY: US 1994-226168 19940412.
AB Disclosed is a method of obtaining an autologous monoclonal antibodies (AMABs) to a self-antigens or homologs from an non-human vertebrate animal. The method comprises (a) altering the genome of the animal so that it does not produce at least one epitope of the self antigen, (b) immunizing the animal with the self antigen or a homolog, (c) collecting from the animal cells produced in response to, and expressing antibodies against, the self antigen or its homolog, and (d) producing antibodies using the collected cells or genetic material derived from the cells. In example, gene targeting of the Cδ gene was performed, IgD-deficient mice was generated, mouse-anti-mouse-IgD monoclonal antibodies was produced, conjugated and used for staining mouse spleen cells. In addition, neural cell adhesion mol. (NCAM)-knockout mice were obtained for generating high affinity AMABs to NCAM.

L16 ANSWER 105 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1995:510475 Document No. 123:421 Delivery of antisense oligodeoxyribonucleotides against the human epidermal growth factor receptor into cultured KB cells with liposomes conjugated to folate via polyethylene glycol. Wang, Susan; Lee, Robert J.; Cauchon, Greg; Gorenstein, David G.; Low, Philip S. (Dep. of Chemistry, Purdue Univ., West Lafayette, IN, 47907, USA). Proceedings of the National Academy of Sciences of the United States of America, 92(8), 3318-22 (English) 1995. CODEN: PNASA6. ISSN: 0027-8424. Publisher: National Academy of Sciences.

AB Antisense oligodeoxyribonucleotides targeted to the epidermal growth factor (EGF) receptor were encapsulated into liposomes linked to folate via a polyethylene glycol spacer (folate-PEG-liposomes) and efficiently delivered into cultured KB cells via folate receptor-mediated endocytosis. The oligonucleotides were a phosphodiester 15-mer antisense to the EGF receptor (EGFR) gene stop codon (AEGFR2), the same sequence with three phosphorothioate linkages at each terminus (AEGFR2S), a randomized 15-mer control of similar base composition to AEGFR2 (RC15), a 14-mer control derived from a symmetrized Escherichia coli lac operator (LACM), and the 5'-fluorescein-labeled homologs of several of the above. Cellular uptake of AEGFR2 encapsulated in folate-PEG-liposomes was nine times higher than AEGFR2 encapsulated in nontargeted liposomes and 16 times higher than unencapsulated AEGFR2. Treatment of KB cells with AEGFR2 in folate-PEG-liposomes resulted in growth inhibition and significant morphol. changes. Curiously, AEGFR2 and AEGFR2S encapsulated in folate-PEG-liposomes exhibited virtually identical growth inhibitory effects, reducing KB cell proliferation by >90% 48 h after the cells were treated for 4 h with 3 μM oligonucleotide. Free AEGFR2 caused almost no growth inhibition, whereas free AEGFR2S was only one-fifth as potent as the folate-PEG-liposome-encapsulated oligonucleotide. Growth inhibition of the oligonucleotide-treated cells was probably due to reduced EGFR expression because indirect immunofluorescence staining of the cells with a monoclonal antibody against the EGFR showed an almost quant. reduction of the EGFR in cells treated with folate-PEG-liposome-entrapped AEGFR2. These results suggest that antisense oligonucleotide encapsulation in folate-PEG-liposomes promise efficient and tumor-specific delivery and that phosphorothioate oligonucleotides appear to offer no major advantage over native phosphodiester DNA when delivered by this route.

L16 ANSWER 106 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1996:101657 Document No. 124:193621 Immunoliposome-mediated targeting of anti-cancer drugs in vivo. Allen, T. M.; Ahmad, I.; Lopes de Menezes, D. E.; Moase, E. H. (Dep. Pharmacology, Univ. Alberta, Edmonton, AB, T6G 2H7, Can.). Biochemical Society Transactions, 23(4), 1073-9 (English) 1995. CODEN: BCSTB5. ISSN: 0300-5127. Publisher: Portland Press.

AB Our expts. to date suggest that immunoliposome-mediated targeting of anti-cancer drugs may be useful in the treatment of newly established micrometastatic disease or metastatic cells migrating in blood of lymph. Furthermore, they appear to have therapeutic efficacy in the treatment of hematol. disorders, where easy access of the immunoliposomes to the diseased cells is possible.

L16 ANSWER 107 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1996:124342 Document No. 124:219976 Cardioprotection by liposome-conjugated sialyl Lewisx-oligosaccharide in myocardial ischemia and reperfusion injury. Murohara, Toyoaki; Margiotta, John; Phillips, Laurie M.; Paulson, James C.; DeFrees, Shawn; Zalipsky, Samuel; Guo, Luke S. S.; Lefer, Allan M. (Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA, 19107, USA). Cardiovascular Research, 30(6), 965-74 (English) 1995. CODEN: CVREAU. ISSN: 0008-6363. Publisher: Elsevier.

AB Selectins are important adhesion mols. which utilize a carbohydrate ligand such as sialyl Lewisx (SLex). The authors objective was to study the effects of a liposome-conjugated SLex (Lipo-SLex) in myocardial ischemia (MI) and reperfusion (R) injury to further clarify the actions of this carbohydrate. The authors studied the efficacy of Lipo-SLex in a feline

model of MI (90 min) and R (270 min) injury in vivo. Lipo-SLex (400 μg SLex/kg, i.v.) was administered i.v. 10 min prior to R. The authors also utilized an in vitro system of neutrophil adherence to thrombin-stimulated coronary endothelium to validate the efficacy of Lipo-SLex. Lipo-SLex significantly attenuated myocardial necrosis (8.6 vs. 29.5 of area-at-risk) and plasma creatine kinase activities compared to vehicle (liposome alone). Moreover, endothelium-dependent relaxation to acetylcholine and A23187 in ischemic-reperfused coronary rings obtained from cats treated with Lipo-SLex was significantly preserved compared to cats given liposomes without SLex. After reperfusion, ex vivo polymorphonuclear leukocyte (PMN) adherence to ischemic-reperfused coronary endothelium was significantly increased in vehicle-treated cats; however, this was significantly attenuated in Lipo-SLex-treated cats (82 vs. 28 PMNs/mm2). Myeloperoxidase activity in the ischemic myocardium, a marker of PMN accumulation, was also significantly attenuated in Lipo-SLex-treated cats compared to liposomes without SLex. Liposome-conjugated SLex-oligosaccharide attenuates myocardial necrosis and preserves coronary endothelial function following MI/R in vivo. The mechanism appears to be mediated by inhibition of the initial PMN-endothelial interaction and eventual accumulation into the ischemic cardiac tissue. The liposome-SLex complex may be an efficient drug formulation for acute inflammatory diseases.

L16 ANSWER 108 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

1995:934393 Document No. 124:15376 A novel strategy affords high-yield coupling of antibody Fab' fragments to liposomes. Shahinian, Serge; Silvius, John R. (Department of Biochemistry, McGill University, Montreal, QC, H3G 1Y6, Can.). Biochimica et Biophysica Acta, 1239(2), 157-67 (English) 1995. CODEN: BBACAQ. ISSN: 0006-3002. Publisher: Elsevier.

AB A new assay for the production of reactive sulfhydryl-bearing antibody Fab' fragments has been utilized to develop conditions affording high efficiencies of coupling of mouse and rabbit IgG-derived Fab' fragments to lipid vesicles containing maleimidyl-functionalized phospholipids. Cysteine and mercaptoethylamine, but not dithiothreitol, reduce antibody F(ab')2 to Fab' fragments in very good yields under conditions where overredn. to heavy and light chains is minimized. Surprisingly, however, a large fraction of the Fab' fragments generated under these conditions can lack maleimide-reactive sulfhydryl groups, as demonstrated using a maleimidyl-poly(ethylene glycol) **conjugate** to shift selectively the electrophoretic mobility of the reactive sulfhydryl-bearing Fab' fragments. After modification of F(ab')2 reduction conditions specifically to maximize the yield of the latter fraction, it is possible to achieve high and very reproducible coupling of functional Fab' fragments to liposomes (equivalent to coupling of ca. 70% of total input protein and almost 100% of the reactive sulfhydryl-bearing Fab' fraction). A novel phospholipid-poly(ethylene glycol)-maleimide 'anchor' allows particularly efficient coupling of Fab' fragments to liposomes, even using relatively low liposome concns. and molar percentages of the liposome-incorporated 'anchor' species. These results demonstrate that with appropriate optimization of the conditions for Fab' production and liposome coupling, Fab' fragments can be coupled to liposomes with efficiencies comparable to or exceeding those reported for coupling of intact antibodies. These results should facilitate the wider use of Fab' fragments as a potentially advantageous alternative to intact antibodies for liposomal targeting in various applications.

L16 ANSWER 109 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

1994:612956 Document No. 121:212956 Maleimidyl PEG derivative of phosphatidylethanolamine for preparation of functionalized pharmaceutical liposomes. Tagawa, Toshiaki; Awane, Kaoru; Nagaike, Kazuhiro (Mitsubishi Kasei Corporation, Japan). Eur. Pat. Appl. EP 607978 A1 19940727, 16 pp. DESIGNATED STATES: R: CH, DE, ES, FR, GB, IT, LI, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1994-100819 19940120. PRIORITY: JP 1993-27651 19930122.

AB A phosphatidylethanolamine derivative comprising dimaleimidyl PEG attached

(via a linker) to the ethanolamine moiety of phosphatidylethanolamine is described. This derivative may be used to prepare liposomes with improved pharmacol. characteristics to which proteins, peptides, sugars, etc. may be attached. A thiol-modified phospholipid was prepared by reaction of iminothiolane and dipalmitoylphosphatidylethanolamine. The thiol derivative was reacted with dimaleimidyl PEG and liposomes were prepared using the product. A monoclonal antibody to a human tumor was conjugated to the resulting liposome. The antibody-**liposome conjugate** displayed affinity for the tumor cells.

L16 ANSWER 110 OF 179 MEDLINE on STN DUPLICATE 29
95098904. PubMed ID: 7800720. A comparison of direct and liposomal antibody **conjugates** of sulfonated aluminum phthalocyanines for selective photoimmunotherapy of human bladder carcinoma. Morgan J; Lottman H; Abbou C C; Chopin D K. (Centre de Recherches Chirurgicales, Creteil, France.) Photochemistry and photobiology, (1994 Nov) 60 (5) 486-96. Journal code: 0376425. ISSN: 0031-8655. Pub. country: United States. Language: English.

AB There is a need to improve the selectivity of photodynamic therapy and for better targeting of tumor cells within specific tumor compartments. Selective in vitro phototoxicity of a human bladder carcinoma cell line 647V has been achieved by targeting sulfonated aluminum phthalocyanines (AlSPc) with monoclonal antibodies. Aluminum tetra-3 sulfonyl chloride phthalocyanine (PC) or rhodamine sulfonyl chloride were directly coupled to antibodies by a sulfonamide linkage and AlSPc or carboxyfluorescein were encapsulated in liposomes of the small unilamellar vesicle type (SUV) bearing antibody. Antibody E7 (IgM subclass), which recognized an antigenic determinant expressed on 647V but was absent on T24 a control human bladder carcinoma cell line, and a control IgM antibody were used. The effects of the two types of **conjugate** were compared. Immunofluorescence studies on living cells demonstrated specific cell surface localization of **conjugates** at 4 degrees C and internalization at 37 degrees C. Phototoxicity was measured by 3-(4,5-dimethylthiazol-2-5-diphenyltetrazolium) bromide assay after exposing AlSPc-sensitized cells to red light. Significant AlSPc dose-dependent phototoxicity of the order 4 degrees C < 4 degrees C plus 37 degrees C < 37 degrees C was observed with E7-SUV and E7-PC in the range 1-8 microM AlSPc. At equimolar AlSPc doses absolute toxicity was similar for the two **conjugate** types, but at equimolar antibody doses, the liposomal **conjugate** was more effective by up to 13-fold. Addition of urine during illumination decreased toxicity, which was attributed to the presence of protective elements. The results suggest that photosensitizers such as AlSPc could be used for antibody-directed therapy and in particular for selectively damaging tumor cells of the epithelial cell compartment in bladder carcinoma by intrabladder administration. The therapeutic ratio, which takes into account both specific and nonspecific toxicity, was greater for the **liposome conjugate** than for the direct **conjugate** indicating their greater suitability for in vivo instillation.

L16 ANSWER 111 OF 179 MEDLINE on STN DUPLICATE 30
94288434. PubMed ID: 8017774. Recombinant growth factor gene expression in vascular cells in vivo. Nabel E G; Plautz G E; Nabel G J. (Department of Internal Medicine, University of Michigan Medical Center, Ann Arbor 48109-0688.) Annals of the New York Academy of Sciences, (1994 Apr 18) 714 247-52. Ref: 28. Journal code: 7506858. ISSN: 0077-8923. Pub. country: United States. Language: English.

AB Several issues are important to the use of direct gene transfer as an investigative tool and as a potential therapeutic modality (Table 3). Transfection efficiencies of different vectors must be improved and optimized. Retroviral vectors and DNA **liposome conjugates** currently used in animal models are low-efficiency vectors. Adenoviruses and adenoviral **conjugates** appear promising, but issues related to gene persistence, germ-line transmission, and stability of expression must be explored. Second, the pharmacology or

dose-response properties of recombinant gene expression have not been investigated. It is not currently known how many cells must be transfected in an arterial segment in order to produce a desired biological effect. Our studies suggest that only a small population of cells is required to secrete a recombinant gene product into the local milieu. This gene product may then have local paracrine effects with amplification of the biological response, suggesting a "gain of function." Third, methods must be developed to target recombinant genes specifically to endothelial cells or smooth muscle cells using cell-specific promoters. Finally, gene expression should be regulated through inducible or repressible promoters. Nonetheless, during the past ten years a dramatic expansion in the fields of gene transfer and gene therapy has occurred. We have entered a new era in which molecular genetic techniques are being increasingly used to investigate the pathophysiology of cardiovascular disorders and to design potential therapies for these diseases. Although technical hurdles related to optimization of vectors and regulated gene expression must be solved, molecular genetic approaches will be increasingly used to study and treat cardiovascular diseases.

L16 ANSWER 112 OF 179 MEDLINE on STN DUPLICATE 31
95198580. PubMed ID: 7891590. Neoglycoprotein-liposome and lectin-**liposome conjugates** as tools for carbohydrate recognition research. Yamazaki N; Kodama M; Gabius H J. (National Institute of Materials and Chemical Research, Functional Molecules Laboratory, Ibaraki, Japan.) Methods in enzymology, (1994) 242 56-65. Journal code: 0212271. ISSN: 0076-6879. Pub. country: United States. Language: English.

L16 ANSWER 113 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1994:116840 Document No. 120:116840 Oxymethylene-oxyethylene copolymers **conjugates** with biomolecules. Pitt, Colin G.; Hendren, Wayne (Amgen Inc., USA). Eur. Pat. Appl. EP 576192 A2 19931229, 14 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1993-304638 19930615. PRIORITY: US 1992-900037 19920617.

AB Biol. factors with enhanced biol. activity are prepared by covalently linking a biomol. to ≥1 chains of a synthetic polymer derived from the oxymethylene-oxyethylene copolymer. α-Ethoxy-ω-hydroxy-poly(1,3-dioxolane) (preparation is given) and N,N'-disuccinimidylcarbonate were dissolved in DMF, followed by dropwise addition of dimethylaminopyridine and stirring the mixture for 1 h at room temperature The mixture was then added to anhydrous ether and the precipitate was collected and purified to obtain succinimidyl α-ethoxy-poly(1,3-dioxolane)-ω-carbonate (I). I was conjugated to recombinant human granulocyte colony stimulating factor (II) to obtain I.II **conjugate.** I.II **conjugate** was injected s.c. into hamster in a single dose of 100μg protein/kg weight White blood cell levels in I.II-treated animals remained elevated 2 days after dosing, at which time its levels in animals treated with II returned to normal.

L16 ANSWER 114 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1993:656303 Document No. 119:256303 Cosmetic **conjugates** of liposomes with lectins. Jones, Malcolm Norcliff; Lyle, Ian Gardner; Kaszuba, Michael (Unilever PLC, UK; Unilever N. V.; Victoria University of Manchester). Eur. Pat. Appl. EP 566368 A2 19931020, 15 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1993-302870 19930414. PRIORITY: GB 1992-8339 19920415.

AB A cosmetic or hair preparation contains particles (e.g. microcapsules, liposomes) having in the cores therapeutic ingredients and lectins which bind to microorganisms of the skin. The cosmetic controls skin disorders, scalp irritation, and underarm odor.

L16 ANSWER 115 OF 179 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS

RESERVED. on STN DUPLICATE 32

93234729 EMBASE Document No.: 1993234729. Drug delivery using antibody-**liposome conjugates.** Betageri G.V.; Jenkins S.A.; Ravis W.R.. Department of Pharmacal Sciences, School of Pharmacy, Auburn University,Auburn, AL 36849-5503, United States. Drug Development and Industrial Pharmacy 19/16 (2109-2116) 1993.
ISSN: 0363-9045. CODEN: DDIPD8. Pub. Country: United States. Language: English. Summary Language: English.

AB Liposomes bearing surface-attached antibody (L-Ab) were prepared to deliver dideoxyinosine triphosphate (ddITP) to human monocyte/macrophages. A mouse monoclonal antibody (IgG(2a)) was modified using succinimidyl pyridyl dithiopropionate (SPDP) as a heterobifunctional reagent in order to **conjugate** the Ab to liposomes through a covalent (thioether) bond. SPDP-modified antibody was incubated with liposomes containing 5 mol% of maleimido phenyl butyrate phosphatidyl ethanolamine (MPB-PE) at room temperature for 8 hr. L-Ab was separated from free and aggregated antibodies by density gradient technique using metrizamide. Uptake of L-Ab by human monocyte/macrophages was measured as a function of time and compared to liposomes prepared with and without MPB-PE and free ddITP. The uptake increased with time with all samples except for free ddITP after 4 hr. This could be explained by dephosphorylation of ddITP. Uptake of MPB-PE liposomes was 2.7 times higher than those without MPB-PE after 48 hr. However, the uptake of L-Ab was 7 times higher than MPB-PE liposomes, 19 times higher than liposomes without MPB-PE, and 80 times higher than free ddITP after 48 hr. It can be concluded that the delivery of ddITP can be increased by surface attached antibody.

L16 ANSWER 116 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

1994:293475 Document No. 120:293475 Neoglycoprotein-**liposome conjugates** for studies of membrane lectins. Yamazaki, N.; Gabius, S.; Kojima, S.; Gabius, H. J. (Funct. Mol. Lab., Natl. Inst. Mater. and Chem. Res., Tsukuba, 305, Japan). Lectins Glycobiol., 319-26. Editor(s): Gabius, Hans-Joachim; Gabius, Sigrun. Springer: Berlin, Germany. (English) 1993. CODEN: 59SGAW.

AB This paper outlines the preparation, characterization, and selected application of neoglycoprotein-**liposome conjugates** which are instrumental in anal. of cell surface lectins.

L16 ANSWER 117 OF 179 MEDLINE on STN DUPLICATE 33

93312838. PubMed ID: 8391843. Conjugation of apolipoprotein B with liposomes and targeting to cells in culture. Lundberg B; Hong K; Papahadjopoulos D. (Department of Biochemistry and Pharmacy, Abo Akademi University, Finland.) Biochimica et biophysica acta, (1993 Jul 4) 1149 (2) 305-12. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB Mixed phospholipid/cholesterol (2:1 molar ratio) liposomes were conjugated with native and acetylated apolipoprotein B (apoB), the protein part of low density lipoprotein (LDL). The objective was to increase the specificity of the cellular uptake of liposomes by utilization of the LDL and scavenger receptor pathways. The method of choice for the conjugation of liposomes with apoB proved to be the detergent solubilization and removal procedure. Two detergents were tested;sodium cholate (NaC) and octyl glucoside (OG). The integrity of the resulting complexes was demonstrated by Sepharose CL-4B gel chromatography and Metrizamide gradient centrifugation. The **conjugates** showed a good physical stability and the leakiness was only marginally larger than for unconjugated liposomes. The interaction of apoB- and acetyl apoB-**liposome conjugates** with CV-1 and J774 cells, respectively, was monitored by an encapsulated pH-sensitive fluorophore, pyranine (8-hydroxy-1,3,6-pyrenetrisulfonate (HPTS)). This dye provides means of detecting binding and endocytosis of **conjugates** in living cells. The internalization was a fast process and about 10-times faster for the OG-**conjugates** than for the corresponding unconjugated liposomes. The **conjugates** showed a clear concentration-dependent association of dye with cells, while this was less

prominent with liposomes. The uptake was nearly an order of magnitude faster with CV-1 cells than with J774 cells. Acidification of intracellular **conjugates** proceeded fast during the first 30 min of incubation and reached a minimum value of approx. pH 6 after 3 h. The specificity of binding of apoB-**liposome conjugates** to CV-1 cells was demonstrated by displacement experiments with native LDL. The results indicate that apoB-**liposome conjugates** may be used as a delivery vehicle for bioactive subtsances to cells.

L16 ANSWER 118 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1994:116527 Document No. 120:116527 Preparation of streptavidin liposomes for use in ligand-specific targeting applications. Loughrey, Helen C.; Choi, Lewis S.; Wong, Kim F.; Cullis, Pieter R.; Bally, Marcel B. (Dep. Biochem., Univ. Coll. Galway, Galway, Ire.). Liposome Technol. (2nd Ed.), Volume 3, 163-78. Editor(s): Gregoriadis, Gregory. CRC: Boca Raton, Fla. (English) 1993. CODEN: 59PWAV.
AB A review, with 28 refs. Noncovalent and covalent coupling of streptavidin, characterization of streptavidin-**liposome conjugates**, targeting of streptavidin liposomes, and in vivo properties of liposomes are discussed.

L16 ANSWER 119 OF 179 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 34
93242415 EMBASE Document No.: 1993242415. Stability of antibody-bearing liposomes containing dideoxyinosine triphosphate. Betageri G.V.; Burrell L.S.. Department of Pharmacal Sciences, School of Pharmacy, Auburn University,Auburn, AL 36849-5503, United States. International Journal of Pharmaceutics 98/1-3 (149-155) 1993.
ISSN: 0378-5173. CODEN: IJPHDE. Pub. Country: Netherlands. Language: English. Summary Language: English.
AB Liposomes bearing surface-attached antibody were prepared to study the retention of dideoxyinosine triphosphate (ddITP). Liposomes of various lipid composition were prepared and conjugated with modified mouse monoclonal antibodies. The antibody (H-2-K(k)) used in this study is for Fc-mediated targeting. Antibody specificity was measured by studying the binding of antibody-**liposome conjugates** to antimouse IgG-Sepharose. The binding of antibody-**liposome conjugates** (L-Ab) was maximum when negatively charged liposomes (DMPC:CHOL:DCP) were employed. Inclusion of cholesterol to DMPC liposomes increased the binding by 4%. The binding was least when the neutral phospholipid compositions were employed (DMPC, DPPC and DMPC:CHOL) to prepare liposomes. The retention of ddITP was measured in plain liposomes and antibody-bearing liposomes stored at 4, 25 and 37°C. The leakage was maximal in DMPC liposomes. Only 20% of ddITP was retained in DMPC liposomes stored at 4°C after a month. However, when samples were stored at 25 and 37°C the retention was 12% and 4% respectively. There was no leakage of ddITP at 4 and 25°C in liposomes prepared using DMPC:CHOL (1:1 mole ratio) and DMPC:CHOL:DCP (7:2:1 mole ratio). The retention of ddITP was significantly increased in DMPC and DPPC liposomes after conjugation with antibodies. The retention of ddITP in DMPC:CHOL and DMPC:CHOL:DCP liposomes conjugated with antibodies was comparable to plain liposomes. These results suggest that the lipid composition used in the preparation of liposomes affect the conjugation of antibodies to liposomes and also the retention of an encapsulated drug.

L16 ANSWER 120 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1993:406723 Document No. 119:6723 Lyophilized liposomes as shelf items for the preparation of immunogenic liposome-peptide **conjugates.**
Friede, M.; Van Regenmortel, M. H. V.; Schuber, F. (Lab. Chim. Bioorg., Univ. Louis Pasteur, Illkirch, F-67400, Fr.). Analytical Biochemistry, 211(1), 117-22 (English) 1993. CODEN: ANBCA2. ISSN: 0003-2697.
AB The conjugation of peptides to liposomes, while relatively simple, represents a tech. hurdle to some labs. wishing to use such liposomes as vehicles to render peptides immunogenic. For such labs., having liposomes

available as shelf items instead of having to prepare liposomes each time they are required may make liposomes more attractive. In this paper it is reported that small unilamellar liposomes bearing maleimide groups at their surface, and containing the adjuvant monophosphoryl lipid A, can be lyophilized and stored without loss of functionality or biol. activity. On rehydration, peptides bearing cysteine residues are readily attached and the resulting **conjugates** exhibit the same immunogenicity as freshly prepared liposomes. These constructs avoid the use of protein carriers and also the use of Freund's adjuvant for raising antibodies against peptides.

L16 ANSWER 121 OF 179 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
1994:9314 Document No.: PREV199497022314. Methotrexate inhibits lipopolysaccharide induced rise in plasma interleukin-1. Williams, Anwen S.; Camilleri, J. P.; Amos, N.; Williams, B. D.. Rheumatol. Res., UWCM, Heath Park, Cardiff, UK. Arthritis and Rheumatism, (1993) Vol. 36, No. 9 SUPPL., pp. S110.
Meeting Info.: 57th Annual Scientific Meeting of the American College of Rheumatology. San Antonio, Texas, USA. November 7-11, 1993.
CODEN: ARHEAW. ISSN: 0004-3591. Language: English.

L16 ANSWER 122 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1993:87547 Document No. 118:87547 Fc-receptor-mediated targeting of antibody-bearing liposomes containing dideoxycytidine triphosphate to human monocyte/macrophages. Betageri, G. V.; Black, C. D. V.; Szebeni, J.; Wahl, L. M.; Weinstein, J. N. (Natl. Cancer Inst., Bethesda, MD, 20892, USA). Journal of Pharmacy and Pharmacology, 45(1), 48-53 (English) 1993. CODEN: JPPMAB. ISSN: 0022-3573.
AB Liposomes bearing surface-attached antibody (L-Ab) mols. can be used for various purposes including the immunospecific delivery of drugs or other materials to antigenic target cells. In this study, L-Ab were prepared to deliver an anti-human immunodeficiency virus (HIV) drug, dideoxycytidine triphosphate (ddCTP) to human monocyte/macrophages. Cells of the monocyte/macrophage lineage are an important reservoir of HIV-1. A mouse monoclonal antibody IgG2a was labeled with 125I and modified using N succinimidyl-3-(2-pyridyldithio)propionate (SPDP) as a heterobifunctional reagent in order to **conjugate** with liposomes to produce a covalent bond (thioether). SPDP-modified antibody was incubated with liposomes containing 5 mol% of maleimido Ph butyrate phosphatidylethanolamine (MPB-PE) at room temperature (21°) for 24 h. L-Ab were separated from free and aggregated antibodies by centrifugation. L-Ab were characterized by measuring particle size and binding to anti-mouse IgG-sepharose. Ninety five per cent of the liposomal (L-Ab) lipid label was bound to anti-mouse IgG-sepharose, whereas only 7% of plain liposomes were bound, indicating non-specific binding. Uptake of L-Ab was measured in human monocyte/macrophages as a function of time and compared with that of plain liposomes. The uptake increased with time and it was 4-6 times greater than that of plain liposomes although part of that effect may have been due to unreacted MPB groups.

L16 ANSWER 123 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1993:120468 Document No. 118:120468 2',3'-dideoxyinosine (ddI) immunoassays, derivatives, **conjugates** and antibodies. Stenglein, Kenneth J.; Murray, Dennis M. (Sigma Chemical Co., USA). PCT Int. Appl. WO 9222639 A1 19921223, 69 pp. DESIGNATED STATES: W: AU, CA; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US4915 19920611. PRIORITY: US 1991-717614 19910619.
AB AIDS therapeutic ddI is determined in samples (biol. fluids) by immunoassay using labeled ddI analogs and antibodies to ddI prepared by using ddI analog as immunogens; preparation of the analogs and antibodies are described. Diagnostic kits for the immunoassays are also disclosed. DdI was reacted with methyl-5-bromovalerate in sieve-dried N,N-dimethylacetamide and methanolic NaOMe, the product was hydrolyzed, and the acid product was conjugated with bovine serum albumin (BSA) or horseradish peroxidase. Rabbits were immunized with the ddI analog-BSA **conjugate**

emulsified with Freund's complete adjuvant. DdI was assayed by EIA using the peroxidase-ddI analog **conjugate** and rabbit antiserum.

L16 ANSWER 124 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1993:35208 Document No. 118:35208 Melanin-based agents for image enhancement in MRI or other imaging procedures. Williams, Robert F. (University of Texas System, USA). PCT Int. Appl. WO 9218166 A1 19921029, 127 pp. DESIGNATED STATES: W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US3177 19920415. PRIORITY: US 1991-685937 19910415.
AB Image-enhancing agents are disclosed which comprise paramagnetic melanin combined with an essentially nondissociable signal-inducing metal. The signal-inducing metal has an association constant for its melanin combination of ≥1020. Upon suspension or dissoln. in water, the metal remains undissocd. A preferred signal inducing metal is (super)paramagnetic (e.g. Fe, Ni, Cu, Er, Eu, Pr, Dy, Ho, Cr, Mn, especially Gd) for MRI. The metal is incorporated into the melanin in an ionic or particulate form. Metals may be used which are especially useful to modify ultrasound images by the enhancement of the image obtained from emission and detection of high-frequency soundwaves. Metals emitting γ-particles (e.g. 51Cr, 68Ga, 99mTc, 111In) may also be used to enhance images from γ-particle emission scanning. Addnl., native or synthesized melanin in and of itself is an effective MRI image-enhancing agent because of the ability to control the free-radical content of the melanin polymers. Gd-melanin complexes were synthesized using various melanin precursors (e.g. L-DOPA) and with different catalysts and solubilization methods. There was no simple relationship between the amount of metal included in the melanin and the relaxation of the melanin. Coupling of Gd-melanin to a monoclonal mouse anti-albumin IgG2a is also described. In imaging expts. in mice, bowel MRI was greatly enhanced by the Gd-melanin. Results of use of Gd-melanin in imaging expts. with rabbits are also reported.

L16 ANSWER 125 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1992:608462 Document No. 117:208462 Apparatus and methods for using hemozoin. Sammons, David W.; Nalbandian, Robert M. (Arizona Technology Development Corp., USA). PCT Int. Appl. WO 9214149 A1 19920820, 49 pp. DESIGNATED STATES: W: AU, CA, HU, JP, KR, PL, RU; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US819 19920131. PRIORITY: US 1991-649689 19910201; US 1991-766622 19910926.
AB Hemozoin was purified from a lysate of Plasmodium falciparum. Mice were immunized i.p. with hemozoin in phosphate-buffered saline (control), hemozoin mixed with CTMO-1 monoclonal antibody to a surface component of ovarian or breast cancer, or hemozoin mixed with rabbit anti-mouse erythrocyte monoclonal antibody. Blood samples were withdrawn from the mice and examined under a light microscope with and without polarized light. In vivo specificity was determined by visualizing the birefringent hemozoin bound to the red cells in the blood samples. An apparatus for analyzing blood samples for white blood cell, red blood cell, and platelet count is also described.

L16 ANSWER 126 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1992:578290 Document No. 117:178290 Therapeutic suppression of specific immune responses by administration of antigen-competitive **conjugates.**. Dintzis, Howard M.; Dintzis, Renee Z. (Johns Hopkins University, USA). U.S. US 5126131 A 19920630, 13 pp. Cont. of U.S. Ser. No. 869,808, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1988-248293 19880921. PRIORITY: US 1983-460266 19830124; US 1986-869808 19860529.
AB Undesired immune responses are suppressed by administering a nonimmunogenic material which comprises one or more haptens or epitopes corresponding to the antigen which causes the undesired immune response

and the number and spacing of the haptens or epitopes are insufficient to trigger an immune response but sufficient to inhibit it. Also disclosed is an improved vaccine from which low-mol. weight suppressive polymer is removed. Thus, a linear polyacrylamide substituted with dinitrophenyl hapten was prepared and its antibody response in mice was observed Treatment of multiple sclerosis, myasthenia gravis, autoimmune thyroiditis, and penicillin hypersensitivity with the hapten **conjugate** was proposed.

L16 ANSWER 127 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1992:658048 Document No. 117:258048 Immunomagnetic particle induced lysis of antibody-conjugated liposomes. Wright, Stephen E.; Huang, Leaf (Dep. Biochem., Univ. Tennessee, Knoxville, TN, 37996-0840, USA). Journal of Liposome Research, 2(2), 257-73 (English) 1992. CODEN: JLREE7. ISSN: 0898-2104.
AB Liposomes of dioleoylphosphatidylethanolamine were prepared (DOPE) and stabilized by addition of 9-12 mol% N-biotinylphosphatidylethanolamine (PE). Liposomes composed of DOPE/N-biotinyl-PE are quite stable and non-leaky although they exhibit strong temperature-dependent leakage following incorporation of palmitylated murine monoclonal antibodies as a targeting ligand. Addition of magnetic chromium dioxide particles coated with anti-mouse antibody to these immunoliposomes lead to their aggregation and the release of entrapped calcein. The lytic event was biphasic with an initial rapid release of 20% dye within 5 min. followed by a slower rate which reached nearly 40% release after 80 min. The rapid release phase was dependent upon the concentration of the liposomes and that of the multivalent particles. Lysis was immunospecific since no release was observed upon addition of nonspecific immunomagnetic particles to the immunoliposomes or if no antibody was incorporated into the liposome. Lysis could also be blocked by the addition of free murine antibody to the solution The ability of these liposomes to release their contents in response to binding a multivalent antigen validates their potential for therapeutic or diagnostic applications.

L16 ANSWER 128 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1992:46219 Document No. 116:46219 Studies on carbohydrate-binding proteins using liposome-based systems. I. Preparation of neoglycoprotein-conjugated liposomes and the feasibility of their use as drug-targeting devices. Yamazaki, Noboru; Kojima, Shuji; Gabius, Sigrun; Gabius, Hans Joachim (Ind. Prod. Res. Inst., Agency Ind. Sci. Technol., Tsukuba, 305, Japan). International Journal of Biochemistry, 24(1), 99-104 (English) 1992. CODEN: IJBOBV. ISSN: 0020-711X.
AB Five types of neoglycoprotein-coupled liposomes were prepared in order to investigate their potential utility as new types of drug-targeting devices which exploit cellular functions of carbohydrate-binding proteins. These prepns. were stable at 37° for 24 h and at 7° over 4 mo. An inhibition assay in an in vitro system using human adenocarcinoma cells indicated the high affinity binding of neoglycoprotein-conjugated liposomes. The inhibitory potency correlated with both the type and the amount of immobilized neoglycoproteins on liposomes. A tissue distribution assay in an in vivo system using Ehrlich solid tumor-bearing mice showed the feasibility of the application of [125I]neoglycoprotein-conjugated liposomes as drug-targeting devices, based on carbohydrate-protein interactions.

L16 ANSWER 129 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1992:230931 Document No. 116:230931 Preparation of polyaminopolycarboxylic acids and their chelation with metals, for use as contrast agents. Elgavish, Garbriel A.; Kim, Sung K. (Research Corp. Technologies, Inc., USA). PCT Int. Appl. WO 9114178 A1 19910919, 38 pp. DESIGNATED STATES: W: CA, JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1991-US1633 19910311. PRIORITY: US 1990-492519 19900312.

AB The polyaminopolycarboxylic acids [R1(CHR)b][R2(CHR)b]NCH2[CH2N[(CH2)bX]CH 2]aCH2N[(CH2R)bR3][(CH2R)bR4] (R = H, alkyl, OH, halo, alkoxy, aryl, aralkyl; R1-R4, X = H, OH, CO2H, R5CO2, etc.; R5 = C6-30 hydrocarbyl; ≥1 R1-R4 or X = R5CO2; a = 0, 1-5; b = 1-5) are prepared and complexed with metal ions (atomic number 21-29, 42-44, 57-83) to give contrast agents, especially useful for NMR.
N,N-Bis(benzyloxycarbonylmethyl)bromoacetami
de (preparation given) was reacted with N,N-bis(2-hydroxyethyl)ethylenediamine in Et3N-containing DMF, to give an intermediate, which upon treatment with myristoyl chloride, in dimethylaminopyridine-containing benzyl chloroformate, gave N-(myristoyloxyethyl)-N'-(2-benzyloxycarbonyloxyethyl)-N,N-bis[N'',N''-bis(benzyloxycarbonylmethyl)acetamido]-1,2-ethanediamine. This was hydrogenated over Pd/C, in EtOH, to give N-(2-myrisotyloxyethyl)-N'-(2-hydroxyethyl)-N,N'-bis[N'',N''-bis(carboxymethyl)acetamido]-1,2-ethanediamine (I). I was complexed with GdCl3·6H2O and the 1:1 I-Gd+3 complex was incorporated into liposomes. The suitability of the complex as a contrast agent was demonstrated by NMR relaxivity measurements.

L16 ANSWER 130 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1991:512642 Document No. 115:112642 Interfacial condensation of bioactive compounds and site-specific compounds such as monoclonal antibodies and **conjugates** thereof. Wrasidlo, Wolfgang J. (Brunswick Corp., USA). PCT Int. Appl. WO 9105806 A1 19910502, 52 pp. DESIGNATED STATES: W: AU, CA, JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1990-US5544 19901002. PRIORITY: US 1989-419337 19891010.
AB A method is provided for preparation of **conjugates** of bioactive compds. and site-specific compds. in which covalent bonding between the compds. is effected by interfacial condensation while protecting the active binding sites from the condensation reaction. This provides very high yields of the **conjugate**, and the products are homogeneous. The method is especially useful for preparation of **conjugates** of monoclonal antibodies (MAbs) with cytotoxic agents. Thus, cis-retinoic acid was reacted with N-hydroxysuccinimide and dimethylaminopropyl Et carbodiimide, and a suspension of the solid intermediate formed was added in excess mol ratio to an aqueous solution of MAb 9.2.27. With vigorous mixing of the solid and aqueous phases to promote the interfacial condensation reaction, the initial very cloudy suspension gradually closed until there was a residual, slightly cloudy suspension of solid succinimic intermediate
precipitate
The suspension was centrifuged, and the product **conjugate** in the aqueous phase was purified by gel chromatog. The **conjugate** had 3 mol retinoic acid per mol MAb. The **conjugate** showed substantially the same binding activity and specificity as the original MAb. Preparation of MAb **conjugates** with methotrexate, with doxorubicin, etc. are described.

L16 ANSWER 131 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1991:510030 Document No. 115:110030 Targeted liposomes and methods using derivatized lipids for liposome-protein coupling. Loughrey, Helen C.; Cullis, Pieter R.; Bally, Marcel B.; Choi, Lewis S. L.; Wong, Kim F. (Liposome Co., Inc., USA). PCT Int. Appl. WO 9100289 A2 19910110, 103 pp. DESIGNATED STATES: W: AU, CA, JP, KR; RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1990-US3582 19900622. PRIORITY: US 1989-370650 19890623; US 1989-412779 19890926.
AB A method is provided for synthesis of a substantially pure reactive lipid including, e.g. N-[4-(p-maleimidophenyl)-butyryl]phosphatidylethanolamine (MPB-PE) and related compns. The compns. are useful as coupling agents and may be incorporated into liposomes and subsequently coupled to proteins, cofactors, etc. A preferred coupling method to disclosed, as are protein **conjugates.** Also provided is a method of preparing sized protein-**liposome conjugate** compns. The protein-**liposome conjugates** are preferably 75-200 nm in size. The liposomes of the invention may have a trans-membrane potential across

the membrane and may be dehydrated. The composition may contain ionizable bioactive agents, e.g. antineoplastic agents, and may be used in diagnostic assays. Thus, dipalmitoyl PE(DPPE) was reacted with N-succinimidyl-4-(p-maleimidophenyl)butyrate to form MPB-DPPE, which was then used in liposome preparation Streptavidin was thiolated, then coupled with the liposomes. Incubation of liposome-streptavidin **conjugates** (containing encapsulated carboxyfluorescein) with a blood leukocyte sample prelabeled with a biotinylated monoclonal antibody (MAb) specific for B-cells or for T-cells gave fluorescein labeling of approx. 20% or approx. 90%, resp., of the total lymphocyte population, which was consistent with the expected cell distribution of the antigens defined by the MAbs.

L16 ANSWER 132 OF 179 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
1992:40082 Document No.: PREV199242016232; BR42:16232. FC-RECEPTOR MEDIATED DELIVERY OF ANTIBODY-**LIPOSOME CONJUGATES** CONTAINING DIDEOXYINOSINE TRIPHOSPHATE TO HUMAN MONOCYTE-MACROPHAGES. BETAGERI G V [Reprint author]; JENKINS S A; RAVIS W R. SCH PHARM, AUBURN UNIV, AUBURN, ALA 36849-5503. Pharmaceutical Research (New York), (1991) Vol. 8, No. 10 SUPPL, pp. S190.
Meeting Info.: AAPS (AMERICAN ASSOCIATION OF PHARMACEUTICAL SCIENTISTS) SIXTH ANNUAL MEETING AND EXPOSITION, WASHINGTON, D.C., USA, NOVEMBER 17-21, 1991. PHARM RES (N Y).
CODEN: PHREEB. ISSN: 0724-8741. Language: ENGLISH.

L16 ANSWER 133 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1991:162071 Document No. 114:162071 Parameters affecting the immunogenicity of a liposome-associated synthetic hexapeptide antigen. Frisch, Benoit; Muller, Sylviane; Briand, Jean Paul; Van Regenmortel, Marc H. V.; Schuber, Francis (Fac. Pharm., Univ. Louis Pasteur Strasbourg, Illkirch, F-67400, Fr.). European Journal of Immunology, 21(1), 185-93 (English) 1991.
CODEN: EJIMAF. ISSN: 0014-2980.
AB The effect of liposome association on the immunogenicity of the hexapeptide IRGERA was investigated. When administered in the absence of a carrier and adjuvant this peptide, which corresponds to a linear epitope located at the C-terminus of histone H3, was not immunogenic. When mice were immunized with peptide (with either GG or CG added to facilitate binding) covalently linked to the surface of small unilamellar vesicles containing monophosphoryl lipid A as adjuvant, a relatively long-lasting response with memory cell induction was observed The anti-peptide antibodies raised in this way reacted with the cognate sequence in the native histone. In contrast, coupling of the peptide to the surface of large vesicles yielded both an IgM and IgG response of short duration whereas encapsulation of the free peptide in large vesicles was ineffective. These results indicate that with short synthetic peptides, liposomes provide a substitute for a carrier protein. However, an adjuvant has to be incorporated in the vesicles in order to obtain an efficient immune response. Such an approach may be useful for designing synthetic vaccines.

L16 ANSWER 134 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1991:602736 Document No. 115:202736 Membrane affinity purification apparatus and its use in the purification of macromolecules of therapeutic value. Goffe, Randal A.; Zale, Stephen E.; O'Connor, James L.; Kessler, Stephen B.; Cohen, Charles M. (Sepracor, Inc., USA). PCT Int. Appl. WO 9005018 A1 19900517, 142 pp. DESIGNATED STATES: W: AU, BB, BG, BR, DK, FI, HU, JP, KR, LK, MC, MG, MW, NO, RO, SD, SU; RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, FR, GA, GB, IT, LU, ML, MR, NL, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1989-US4847 19891030. PRIORITY: US 1988-265061 19881031.
AB An apparatus is provided which is useful for the separation of ≥1 preselected ligate(s) in a fluid. Also provided is an easily scaled-up membrane affinity separation process which is reliable, highly selective, gives a high yield of product, and has a high volumetric throughput. A substantially isotropic porous membrane is used, to which is associated a preselected

ligand, which provides an optimum loading capacity and low dead volume while allowing high filtrate flow rates. Methods for isolation of macromols. of therapeutic value, e.g. factor VIII and fibronectin, are described, and diagrams of the apparatus are included. Cloning and expression of a bifunctional binding site protein (one domain binding digoxin and the other binding Ig Fc regions) are also described. Thus a polyether sulfone/poly(ethylene oxide) hollow-fiber membrane was sequentially reacted with ethylene glycol diglycidyl ether and hydroxyethyl cellulose, activated with 2-fluoro-1-methylpyridinium p-toluenesulfonate, and the activated fibers reacted with an antibody to factor VIII. The resulting membrane was used to purify a factor VIII concentrate; the purification factor was 115.

L16 ANSWER 135 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1990:545333 Document No. 113:145333 Vasopermeability-enhancing agent **conjugates** with delivery agents, and their use at a tumor site for enhanced delivery of diagnostic or therapeutic agents. Epstein, Alan L.; Glovsky, Michael M. (University of Southern California, USA). PCT Int. Appl. WO 9003801 A1 19900419, 48 pp. DESIGNATED STATES: W: AU, JP; RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1989-US4513 19891011. PRIORITY: US 1988-255513 19881011.
AB The title **conjugates** have a clin. useful delivery vehicle, e.g. a monoclonal antibody (MAb) linked to a biol. active species which acts to increase vascular permeability and expand blood volume at or in proximity to the tumor site. The vehicle-linked species may be a vasoactive agent, a substance that recruits or amplifies a vasoactive species, a toxin, an isotope, etc. Chemical and recombinant DNA methods for preparing the **conjugates** are described. A therapy is disclosed which comprises administration of the vasoactive **conjugate** and delivering a diagnostic or therapeutic agent at an optimal time thereafter, when tumor vasculature is maximally expanded. Thus, an immunoconjugate of interleukin-2 (IL-2) linked to a MAb (Lym-1) to lymphoma cells was prepared and tested in lymphoma-bearing nude mice. Animals received either Lym-1 alone or Lym-1 IL-2 immunoconjugate at or before administration of 125I-labeled Lym-1 F(ab')2. Mice receiving the vasoconjugate showed a 200% increase in MAb localization over appropriate controls. The increase in MAb localization enhanced the tumor/blood ratio approx. 2-fold, was dose-dependent (maximum effect at 30-50 μg of vasoconjugate), and was time-dependent (maximum effect at 2 1/2 h prior to administration of the MAb).

L16 ANSWER 136 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1991:108929 Document No. 114:108929 Avidin or streptavidin conjugated liposomes. Hawrot, Edward; Rosenberg, Michael B.; Breakefield, Xandra O. (Yale University, USA). U.S. US 4948590 A 19900814, 22 pp. (English). CODEN: USXXAM. APPLICATION: US 1987-60140 19870609.
AB A liposome is conjugated with a streptavidin compound, wherein carboxyl residues of the streptavidin are coupled to phospholipid amino groups of the liposome. The resultant streptavidin-conjugated liposome can be used to encapsulate drugs and cytotoxic agents for site-specific targeting. For example, liposomes were prepared from lipids by the reverse-phase evaporation method, mixed with streptavidin in a buffer, and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide was added to give liposomes conjugated with streptavidin.

L16 ANSWER 137 OF 179 MEDLINE on STN DUPLICATE 35
90203581. PubMed ID: 1969450. Lymphocyte proliferative responses to soluble and liposome-conjugated envelope peptides of HIV-1. Krowka J; Stites D; Debs R; Larsen C; Fedor J; Brunette E; Duzgunes N. (Department of Laboratory Medicine, University of California, San Francisco 94143.) Journal of immunology (Baltimore, Md. : 1950), (1990 Apr 1) 144 (7) 2535-40. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB The proliferation of lymphocytes from HIV-seronegative (HIV Ab-) and seropositive (HIV Ab+) individuals in response to two synthetic peptide epitopes of HIV envelope glycoproteins (ENVgp) was evaluated as an index of cell-mediated immunity in infected individuals. All HIV Ab- and most HIV Ab+ individuals' lymphocytes failed to proliferate in primary cultures in response to the two soluble HIV ENVgp peptides, ENVP346 and ENVP466 even in the presence of rIL-2. After stimulation with **liposome-conjugates** of ENVP346 or ENVP466 and soluble rIL-2, however, CD4 lymphocytes from some HIV Ab+ individuals were able to proliferate. Significantly higher frequencies of rIL-2-augmented proliferative responses to liposome-conjugated ENVP346 or ENVP466 were observed in HIV Ab+ asymptomatic individuals as compared to patients with AIDS-related conditions or AIDS. These studies indicate that the conjugation of HIV peptides or proteins to liposomes and stimulation with rIL-2 may enhance cell-mediated responses to these peptides.

L16 ANSWER 138 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

1991:17184 Document No. 114:17184 Regulation of distribution, amount and ligand affinity of sugar receptors in human colon carcinoma cells by treatment with sodium butyrate, retinoic acid and phorbol ester. Gabius, Sigrun; Yamazaki, Noboru; Hanewacker, Wiltrud; Gabius, Hans Joachim (Abt. Haematol. - Onkol., Med. Universitaetsklin., Goettingen, D-3400, Germany). Anticancer Research, 10(4), 1005-12 (English) 1990. CODEN: ANTRD4. ISSN: 0250-7005.

AB Human colon carcinoma cells were treated with non-toxic levels of sodium butyrate, retinoic acid phorbol ester, eliciting characteristic growth inhibition and morphol. changes. Since protein-carbohydrate interactions are supposedly involved in regulatory processes and can serve within targeted drug delivery, the capacity to bind components of the carbohydrate chains of cellular glycoconjugates was monitored for such cells in relation to the type of the medium additive. The pattern of binding of a panel of neoglycoproteins was significantly altered for fixed cells, depending on the type of putative maturation factor. Quantitation of cell surface sugar receptors at a non-saturating concentration of neoglycoenzyme, employed as carbohydrate ligand-exposing probe, led to a similar conclusion. Up to six-fold increases were determined for individual probes. Binding studies with varying concns. of neoglycoenzymes in the case of four ligands revealed that the receptor d., but not the affinity was significantly affected. Biochem. analyses corroborated this result by demonstrating mainly quant. differences after affinity chromatog. of detergent exts. from the four types of cell pellet. By showing the inhibitory potency of neoglycoprotein-conjugated liposomes in the cell binding assay with neoglycoenzymes, a perspective is indicated, of how the different effects of the differentiation-inducing agents might be beneficially exploited in targeted drug delivery.

L16 ANSWER 139 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

1991:159993 Document No. 114:159993 MR imaging of pulmonary parenchyma and emboli by paramagnetic and superparamagnetic contrast agents. Thakur, M. L.; Vinitski, S.; Mitchell, D. G.; Consigny, P. M.; Lin, S.; DeFulvio, J.; Rifkin, M. (Thomas Jefferson Univ., Philadelphia, PA, 19107, USA). Magnetic Resonance Imaging, 8(5), 625-30 (English) 1990. CODEN: MRIMDQ. ISSN: 0730-725X.

AB Using exptl. induced pulmonary emboli in an animal model, 3 i.v. administered contrast agents, Gd-DTPA-albumin microspheres (8-15 μm, 0.2M particles/mg protein, 39-106 μg Gd/mg, 50 mg/mL), Gd-DTPA-liposomes (15-30 μm, 130 μg/mg lipid, 6 mg Gd/mL), and superparamagnetic ferrosome, (60 nm, 100 mM Fe and 20 mg lipid/mL) were examined for MR imaging. Gd-DTPA entrapped in lung capillaries did not enhance the signal intensity of lung parenchyma, but liposomes (5 mL) served as better Gd-DTPA carriers and increased the parenchymal signal intensity by 2-3-fold. However, neither agent improved delineation of pulmonary emboli. Ferrosome decreased the intensity of lung parenchyma, improving detectability of pulmonary emboli by several factors.

L16 ANSWER 140 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1991:629825 Document No. 115:229825 A measurement of complement activity using immunoliposome. Kishimura, Masaaki; Yamaji, Hideki; Fukuda, Hideki; Terashima, Masaaki; Katoh, Shigeo; Sada, Eizo; Taniguchi, Hiroshi (Eng. Res. Lab., Kanegafuchi Chem. Ind. Co., Ltd., Takasago, 676, Japan). Annals of the New York Academy of Sciences, 613(Enzyme Eng. 10), 405-9 (English) 1990. CODEN: ANYAA9. ISSN: 0077-8923.

AB A simple method was developed for measuring the complement activities of both the classical and alternative pathways in the same system by using the rabbit γ-globulin-coupled liposomes.

L16 ANSWER 141 OF 179 MEDLINE on STN DUPLICATE 36
91002598. PubMed ID: 2207121. Protein-**liposome conjugates** with defined size distributions. Loughrey H C; Wong K F; Choi L S; Cullis P R; Bally M B. (University of British Columbia, Faculty of Medicine, Department of Biochemistry, Vancouver, Canada.) Biochimica et biophysica acta, (1990 Sep 21) 1028 (1) 73-81. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB Conjugation of protein to liposomes by two coupling protocols is shown to result in vesicle aggregation. The degree of aggregation is directly related to the levels of protein conjugated to the liposomes. In an attempt to develop a method of generating stable, homogeneously sized protein-conjugated vesicles, highly aggregated liposome-protein **conjugates** were extruded through filters of defined pore size distributions, with no loss of protein binding. The extruded samples are relatively stable with respect to size and are easily prepared for various protein to lipid ratios. Liposome size has been shown to be a major factor in determining the in vivo blood circulation times of liposomes. A corresponding, significant enhancement in the blood circulation lifetimes for extruded versus aggregated streptavidin-**liposome conjugates** is observed. Furthermore, the stability of streptavidin-**liposome conjugates** in vivo was shown by the binding of biotin to liposomes isolated from plasma 1 and 4 h post-injection. In conclusion, extrusion of the aggregated systems obtained on coupling proteins to liposomes provides a convenient and general method for generating homogeneously sized protein-**liposome conjugates.**

L16 ANSWER 142 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1990:558683 Document No. 113:158683 Liposomes coupled to hormones for targeted drug delivery. Konigsberg, Paula Jean; Richer, Leroy Leonard; Schmidt, Paul Gardner; Uliana, Joseph Anthony (Sandoz A.-G., Switz.; Vestar, Inc.). PCT Int. Appl. WO 8911270 A1 19891130, 35 pp. DESIGNATED STATES: W: JP; RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1989-EP521 19890512. PRIORITY: US 1988-194636 19880516.

AB Liposomes are coupled to hormones having a cell receptor site, especially a cytokine such as interleukin-2 (IL-2), through a lysine, cysteine, arginine, or histidine residue not in the receptor site. They are coupled by either (a) fixing a coupling agent to the liposome and then reacting with the hormone; (b) fixing a coupling agent to the hormone and reacting with liposomes; or (c) fixing a 1st coupling agent to liposomes, fixing a 2nd coupling agent to the hormone, and then reacting the 2 coupling moieties. The liposomes may be used as delivery vehicles for targeted delivery of a pharmaceutical or diagnostic agent. Thus, IL-2 was conjugated to succinimidyl-4-(p-maleimidophenyl)butyrate (SMPB) through ε-NH2 groups at lysine, on an affinity column containing monoclonal antibody to the IL-2 receptor site. The purified reaction product of succinimidyl-S-acetylthioacetate (SATA) and distearoyl phosphatidylethanolamine (preparation described) was incorporated into liposomes with distearoyl phosphatidylcholine and cholesterol. The SMPB-IL-2 was then conjugated to the liposomes through the interaction of the maleimido groups and the deacetylated SATA residues.

L16 ,ANSWER 143 OF 179 MEDLINE on STN DUPLICATE 37
89336706. PubMed ID: 2788031. Role of ligand in antibody-directed endocytosis of liposomes by human T-leukemia cells. Matthay K K; Abai A M; Cobb S; Hong K; Papahadjopoulos D; Straubinger R M. (Department of Pediatrics, University of California, San Francisco 94143.) Cancer research, (1989 Sep 1) 49 (17) 4879-86. Journal code: 2984705R. ISSN: 0008-5472. Pub. country: United States. Language: English.

AB The rate of uptake and intracellular processing of ligand-directed drug carriers may depend heavily on the endocytic pathway of the target antigen. We examined the role of the target antigen and type of antibody-liposome linkage in determining endocytosis of liposomes by three human T-cell leukemias, Jurkat, CEM, and Molt-4. Liposome-cell binding and internalization over time were studied using two independent assays for intracellular delivery of liposome contents: a new fluorescence assay using a pH-sensitive fluorescent dye; and a growth inhibition assay for delivery of cytotoxic drug, methotrexate-gamma-aspartate. Liposomes targeted against the transferrin receptor showed greater surface binding, internalization, and growth inhibition than liposomes targeted against the T-cell surface antigens, CD2, CD3, or CD5. Furthermore, liposomes made by conjugating the targeting antibody directly to the liposome surface were more efficiently internalized and retained than were liposomes linked to antibody-coated cells via Protein A. Selection of the type of antibody-**liposome conjugate** as well as the appropriate surface receptor to facilitate endocytosis is essential in antibody-directed drug treatment of cancer.

L16 'ANSWER 144 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1990:11839 Document No. 112:11839 Comparison of anti-Tac and anti-transferrin receptor-conjugated liposomes for specific drug delivery to adult T-cell leukemia. Hege, Kristen M.; Daleke, David L.; Waldmann, Thomas A.; Matthay, Katherine K. (Dep. Pediatrics, Univ. California, San Francisco, CA, USA). Blood, 74(6), 2043-52 (English) 1989. CODEN: BLOOAW. ISSN: 0006-4971.

AB Adult T-cell leukemia (ATL) is a rapidly progressive and usually fatal malignancy of mature T cells characterized by the expression of large nos. of interleukin-2 (IL-2) receptors on the cell surface. Anti-Tac, a monoclonal antibody directed against the IL-2 receptor, was conjugated to liposomes and compared with anti-transferrin receptor (anti-TFR) **conjugates** for specific binding, internalization, and intracellular drug delivery to ATL cells. Two independent assays were used: a fluorimetric assay with liposome encapsulated 1-hydroxypyrene-3,6,8-trisulfonic acid, a pH-sensitive fluorescent dye, and growth inhibition assay using methotrexate γ-aspartate, a liposome-dependent cytotoxic drug. MT-1 and HUT-102 cell lines derived from patients with ATL were compared with Molt-4, a leukemia cell line that does not express IL-2 receptors in an uninduced state. Fluorimetric studies showed specific binding and internalization of anti-Tac-conjugated liposomes by HUT-102 and MT-1 but not by the Tac-neg. cell line Molt-4, demonstrating the lack of nonspecific or Fc receptor-mediated uptake. Anti-TFR-conjugated liposomes were effectively bound and internalized by all three cell lines and consistently showed the highest degree of ,cellular liposome uptake. Drug-containing liposomes conjugated to anti-Tac were more than tenfold more effective in causing growth inhibition of ATL cells than the nonspecific control **conjugates.** Anti-Tac **conjugates** caused minimal growth inhibition of Molt-4 cells over the concentration range effective against the ATL cells. Anti-TFR-coupled liposomes gave better growth inhibition of HUT-102 and MT-1 cells (40- to 60-fold) than anti-Tac **conjugates.** Both anti-Tac-directed and anti-TFR-directed liposomes are effective for intracellular drug delivery to ATL cells and may represent a useful method of treatment in this disease.

L16 ANSWER 145 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1989:190223 Document No. 110:190223 Lectin-bearing liposomes: differential

binding to normal and to transformed mouse fibroblasts. Bogdanov, A. A., Jr.; Gordeeva, L. V.; Torchilin, V. P.; Margolis, L. B. (Inst. Exp. Cardiol., Moscow, 121552, USSR). Experimental Cell Research, 181(2), 362-74 (English) 1989. CODEN: ECREAL. ISSN: 0014-4827.

AB The binding of covalent **conjugates** of Con A or wheat-germ agglutinin (WGA) and liposomes (lectin-liposomes) to the surface of normal and transformed mouse fibroblasts was studied. Quantitation of the binding was performed by means of microfluorometry and radioactive lipid label counting using both sparse and dense cell cultures. It was found that 2.5-3 times more lectin-conjugated liposomes are bound to L or SV3T3 cells than to the mouse embryo fibroblasts and 3T3 cells in a broad concentration range. The binding of Con A- and WGA-liposomes was inhibited up to 70% in the presence of the corresponding carbohydrate inhibitors. A decreased binding of lectin-liposomes to cells was also observed when cells were pretreated with the free lectin. Trypsinization of the cells resulted in an increase in the Con A-liposomes binding to normal fibroblasts. When free fluorescent Con A or WGA was used in binding studies, no profound differences in the binding of lectin to normal or transformed cells were detected. The relation of the lectin-liposome/cell to cell/cell interactions is discussed.

L16 ANSWER 146 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

1989:130851 Document No. 110:130851 Analysis of the carbohydrate-binding specificity of lectin-conjugated lipid vesicles which interact with polysaccharide fragments. Yamazaki, Noboru (Ind. Prod. Res. Inst., Agency Ind. Sci. Technol., Tsukuba, 305, Japan). Journal of Membrane Science, 41, 249-67 (English) 1989. CODEN: JMESDO. ISSN: 0376-7388.

AB In order to obtain some insight into understanding of the multivalent interactions between polysaccharide fragments as ligands and lectins conjugated on the membrane surface of lipid vesicles as receptors, two kinds of lectin-conjugated lipid vesicles were prepared, and studies on agglutination and binding were performed with two kinds of microscale assays by applying these to two model systems consisting of different ligands and receptors. The agglutination studies based on the interaction between plant galactomannan fragments and Ricinus communis agglutinin-conjugated lipid vesicles indicated three possible cases of interaction; strong agglutination was caused by large-size fragments with high side chain d., moderate agglutination by medium-size fragments with low side chain d., and no agglutination by small-size fragments. The binding studies based on the interaction between yeast mannan fragments and Con A lectin-conjugated lipid vesicles, together with glycosyl-linkage composition analyses, suggested that binding efficiency should be correlated with the structural characteristics of ligands such as size of fragments, rate of branching, and number of high-affinity residues.

L16 ANSWER 147 OF 179 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

1988:427163 Document No.: PREV198835079293; BR35:79293. PROTEIN-**LIPOSOME CONJUGATES** US PATENT-4762915. AUGUST 9 1988. KUNG V T [Inventor, Reprint author]; REDEMANN C T [Inventor]. MENLO PARK, CALIF, USA. ASSIGNEE: LIPOSOME TECHNOLOGY, INC. Patent Info.: US 4762915 August 09, 1988. Official Gazette of the United States Patent and Trademark Office Patents, (1988) Vol. 1093, No. 2, pp. 799. CODEN: OGUPE7. ISSN: 0098-1133. Language: ENGLISH.

L16 ANSWER 148 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

1989:111334 Document No. 110:111334 Labeled liposome-antibody **conjugates** for determination of specific test substances by complement lysis immunoassay.. Ishimori, Yoshio; Hado, Masako (Toshiba Corp., Japan). Jpn. Kokai Tokkyo Koho JP 63120256 A2 19880524 Showa, 8 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1986-265038 19861107.

AB A hydrophilic label is encapsulated in cholesterol-containing phospholipids or glycolipids and the surface of the capsules is sensitized with a 1st antibody to the test substance via a crosslinking agent. A reagent for immunoassay consists of the sensitized liposomes and a 2nd antibody to the

test substance. For IgG determination, a sample in a microplate was treated with a reagent containing goat anti-human IgG antibody-sensitized, carboxyfluorescein-containing liposomes, a 2nd antibody, and gelatin-veronal buffer at 37° for 30 min, followed by incubation with complement (CH50) at 37° for 1 h, mixing with EDTA-veronal buffer for reaction termination, and fluorometric anal. of released carboxyfluorescein. The detection limit was 10-6-10-8 g/mL.

L16 ANSWER 149 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1988:202816 Document No. 108:202816 Antibodies recognizing human serum albumin are not elicited by immunization with preS2 sequences of the hepatitis B virus envelope protein. Neurath, A. Robert; Strick, Nathan; Parker, Karen; Kent, Stephen B. H. (Lindsley F. Kimball Res. Inst., New York Blood Cent., New York, NY, 10021, USA). Journal of Medical Virology, 24(2), 137-51 (English) 1988. CODEN: JMVIDB. ISSN: 0146-6615.
AB Antibodies to the preS2 region of the hepatitis B virus (HBV) envelope protein and to human serum albumin (HSA) were allegedly detected at about the same level in sera of humans with acute or chronic hepatitis B. It was claimed that anti-HSA arises as a result of an immune response to the preS2 sequence and that it was involved in hepatocellular damage. Over 100 sera from animals and humans immunized with hepatitis surface antigen containing preS2 sequences, or with synthetic peptides from the preS1, preS2, and S regions of the HBV env protein were assayed for anti-HSA. Immunization with the native preS2 sequence or with unconjugated synthetic peptides derived from that sequence does not result in elicitation of anti-HSA. Therefore, the alleged appearance of anti-HSA during hepatitis B cannot be directly related to an anti-preS2-specific immune response. Some synthetic peptides, whether or not they were derived from the preS2 sequence, when linked to certain carriers, but not to others, elicited in rabbits an anti-HSA response, which was markedly lower than the response to the homologous peptide. These anti-HSA antibodies could be separated from anti-preS2-specific antibodies by affinity chromatog. and did not recognize the synthetic peptide used for immunization. The use in active immunoprophylaxis of hepatitis B of unconjugated peptides from the preS2 sequence with proven high immunogenicity will avoid carrier/linker-mediated induction of antibodies not relevant to protection against HBV.

L16 ANSWER 150 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1988:70178 Document No. 108:70178 Transfer of inorganic or organic compounds to animal egg and/or somatic cells using vesicles or granules bound to sperm, and production of transgenic cells and embryos thereby. Rottmann, Oswald; Hoefer, Paul (Transgene G.m.b.H., Fed. Rep. Ger.). PCT Int. Appl. WO 8705325 A1 19870911, 46 pp. DESIGNATED STATES: W: AU, DK, JP, US; RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1987-EP123 19870302. PRIORITY: DE 1986-3606891 19860303; DE 1986-3636991 19861030.
AB A method for transferring organic (e.g. DNA) or inorg. substances to egg cells and/or somatic cells comprises contacting sperm, optionally modified by chemical or phys. means, with vesicles or granules containing said substances.
The transfer may occur in vitro or in vivo (e.g. by artificial insemination), and may be used to produce transgenic animals. A plasmid containing the growth hormone gene was incorporated into rabbit blood cell membrane lipid-containing liposomes, the liposomes coated with concanavalin A (ConA) after neuraminidase digestion (to expose lectin-binding sugar moieties), and the resulting liposomes incubated with sperm. After masking unoccupied lectin binding sites with α-mannose or α-glucose, ovulating rabbits were artificially inseminated with the sperm-**liposome conjugate.** To verify that the gene had been integrated into the genome, embryos at the bicellular to blastocyst stage were washed out of the fallopian tubes or uterus and analyzed by DNA hybridization.

L16 ANSWER 151 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

1988:48811 Document No. 108:48811 Antibody-directed targeting of liposomes to human cell lines: role of binding and internalization on growth inhibition. Berinstein, Neil; Matthay, Katherine K.; Paphadjopoulos, Demetrios; Levy, Ronald; Sikic, Branimir I. (Sch. Med., Stanford Univ., Stanford, CA, 94305, USA). Cancer Research, 47(22), 5954-9 (English) 1987. CODEN: CNREA8. ISSN: 0008-5472.

AB Small unilamellar liposomes containing methotrexate or methotrexate-γ-aspartate were conjugated to Staphylococcus aureus protein A (PA) and were thus able to blind cell-specific Igs for targeting to malignant human B- and T-cell lines. Enhanced PA liposome uptake and growth inhibition by targeting with an anti-major histocompatibility complex class II antibody recognizing 2 different B-cell lines were observed The enhanced growth inhibition was specific for the targeting antibody and amounted to a 2-3-fold lowering of the concentration of drug required to inhibit cell growth by 50% as compared to nontargeted liposomes or liposomes targeted with an antibody not recognizing a cell surface antigen. A strong association between enhanced growth inhibition and liposome internalization as assessed by fluorescent-activated cell sorter anal. of carboxyfluorescein containing PA liposomes was seen. By contrast, specific enhancement of growth inhibition was not seen with several anti-idiotype antibodies or antibodies to T-cell differentiation antigens. Liposome internalization did not occur with these antibodies. Failure of growth inhibition and PA liposome internalization could not be explained by differences in cell binding of the antibody PA liposomes or the degree of PA binding of the targeting antibody. Although the ability of the targeting antibody to bind to the cell and to PA are important, these factors alone are not sufficient to guarantee internalization and growth inhibition. Variations in rates of internalization of various cell surface antigen-antibody complexes may account for different PA liposome-mediated cytotoxicities.

L16 ANSWER 152 OF 179 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

1988:47851 Document No.: PREV198885024710; BA85:24710. DETECTION OF VERY LOW RECEPTOR NUMBERS ON CELLS BY FLOW CYTOMETRY USING A SENSITIVE STAINING METHOD. TRUNEH A [Reprint author]; MACHY P. CENT D'IMMUNOL INSERM-CNRS MARSEILLE-LUMINY, CASE 906, MARSEILLE 13288, CEDEX 9, FRANCE. Cytometry, (1987) Vol. 8, No. 6, pp. 562-567.
CODEN: CYTODQ. ISSN: 0196-4763. Language: ENGLISH.

AB We describe a staining method for flow cytometry that resolves with a high degree of sensitivity very low numbers of cell surface molecules, which are normally too few to detect using the conventional fluorescein-conjugated reagents. We took advantage of the fact that liposomes can be constructed to contain hundreds of thousands of fluorochrome molecules per vesicle; antigen specificity can be conferred by covalently conjugating them to antibodies or protein A. Unlike fluorochromes such as fluorescein isothiocyanate (FITC) that are directly conjugated to protein ligands with a fluorochrome to protein ratio of about 2 to 1 on the average, their large encapsulating capacity gives liposomes a tremendous potential for signal amplification. In an indirect immunofluorescence study using liposomes that contained the fluorochrome carboxyfluorescein (CF) and that were covalently conjugated to protein A, we were able to obtain up to 50 times the fluorescence signal over background that could be detected with FITC-conjugated protein A. Scatchard analysis showed that the thymoma cell line RDM4 expresses 23,000 and 2,600 binding sites for monoclonal antibodies (mAb) against H-2K and H-2D, respectively. When RDM4 cells were treated with anti-H-2K mAb followed by FITC-conjugated protein A, at best we were able to obtain a fluorescence signal that was only 7 times above background. However, when these cells were treated with the same antibody followed by protein A conjugated to small unilamellar liposomes or large unilamellar liposomes, the fluorescence signals were 110 and 335 times above background, respectively. Using the **liposome conjugates**, we were also able to detect with ease the 2,600 binding sites for the anti-H-2D mAb, whereas the FITC **conjugate** failed completely to resolve specific binding from background. We estimate conservatively that by using this methodology, it will be

possible to detect as few as 800 binding sites per cell.

L16 ANSWER 153 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1987:623153 Document No. 107:223153 Preparation and antitumor effect of macrophage activating factor (MAF) encapsulated in liposomes bearing a monoclonal anti-human melanoma (A375) antibody. Watanabe, Yoshifumi; Uchida, Eriko; Higuchi, Masahiro; Imai, Yasuyuki; Osawa, Toshiaki (Fac. Pharm. Sci., Univ. Tokyo, Tokyo, 113, Japan). Journal of Biological Response Modifiers, 6(5), 556-68 (English) 1987. CODEN: JBRMDS. ISSN: 0732-6580.
AB Large unilamellar vesicles were prepared containing the cell-free culture supernatant of a human T cell hybridoma rich in macrophage-activating factor (MAF) and bearing monoclonal antibodies against human melanoma A375 tumor cells; their antitumor activity against A375 cells was examined in vitro and in vivo. Both MAF-immunoliposomes (bearing antibodies) and MAF liposomes (not bearing antibodies) showed macrophage-mediated cytotoxicity in vitro at a high E/T ratio (about 40). But at a low E/T ratio (about 15), only MAF-immunoliposomes showed tumoricidal activity, their activity being >10,000-fold stronger compared with a soluble MAF preparation (MAF solution).
MAF-immunoliposomes not only showed tumor neutralization mediated by macrophages in vivo when a mixture of tumor cells, macrophages, and MAF-immunoliposomes was locally injected, but also showed significant inhibition of tumor growth on repeated i.v. systemic administration of them. Other samples (MAF-liposomes without the antibody, a MAF solution, and immunoliposomes without MAF) were not significantly effective against tumor growth. Thus, the delivery of lymphokines to the tumor sites is important or even critical when an attempt is made to treat cancer with lymphokines with the expectation of the potentiation of the host's immune system.

L16 ANSWER 154 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1987:143861 Document No. 106:143861 Selective killing of T lymphocytes by phototoxic liposomes. Yemul, Shrishailam; Berger, Carole; Estabrook, Alison; Suarez, Sylvia; Edelson, Richard; Bayley, Hagan (Coll. Physicians Surg., Columbia Univ., New York, NY, 10032, USA). Proceedings of the National Academy of Sciences of the United States of America, 84(1), 246-50 (English) 1987. CODEN: PNASA6. ISSN: 0027-8424.
AB Two-fold specificity in drug delivery obtained through the localized activation of drugs by phys. means and the attachment of drugs to proteins that bind to target cells might be used for highly selective cancer chemotherapy or for immunosuppression. Toward this end, a monoclonal antibody against an antigen on the surface of T lymphocytes was covalently attached to liposomes containing a phototoxic drug, pyrene [129-00-0], bound to the lipid bilayer. When unfractionated peripheral blood lymphocytes, or B- and T-cell lines, were irradiated after treatment with these liposomes, T cells were killed while B cells were spared, demonstrating the validity of the approach in a simple in vitro assay.

L16 ANSWER 155 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1988:11092 Document No. 108:11092 Liposomes as carriers of lipophilic cytosine arabinoside- and fluorodeoxyuridine-derivatives. Their cytostatic effect and possibilities for tumor-specific therapy. Schwendener, R. A.; Schott, H.; Hartmann, H. R.; Supersaxo, A.; Rubas, W.; Hengartner, H. (Inst. Pathol., Universitaetssp., Zurich, Switz.). Onkologie, 10(4), 232-9 (German) 1987. CODEN: ONKOD2. ISSN: 0378-584X.
AB A method for the preparation of large vols. of sterile, homogeneous bilayer liposomes as carriers of lipophilic cytostatic prodrugs is described. Liposomes of 60-120-nm diameter were produced by capillary dialysis of lipid-prodrug-detergent micelles. Lipophilic cytosine arabinoside-prodrug liposomes were superior to free cytosine arabinoside against L1210 leukemia cells in mice. Lipophilic fluorodeoxyuridine-prodrug liposomes were active against solid tumors, although with less pronounced effects, at 20-60-fold lower concns. than free fluorodeoxyuridine. Methods for linking tumor-cell-specific antibodies to

liposomes are discussed in order to improve the cytostatic effects of prodrug-containing liposomes.

L16 ANSWER 156 OF 179 MEDLINE on STN DUPLICATE 38
87271672. PubMed ID: 2886152. Targeting of anti-Thy 1.1 monoclonal antibody conjugated liposomes in Thy 1.1 mice after intravenous administration. Debs R J; Heath T D; Papahadjopoulos D. Biochimica et biophysica acta, (1987 Jul 23) 901 (2) 183-90. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.
AB 125I-labeled liposomes, conjugated to an anti-Thy 1.1 monoclonal antibody (MRCOX7), demonstrated up to 7.4-fold greater lymph node uptake than liposomes conjugated to non-specific monoclonal antibody (R-10) after intravenous injection into Thy 1.1 (AKR-J) mice. Uptake of anti-Thy 1.1-conjugated liposomes by the lymph nodes of AKR-J mice was 3-times greater than their uptake by lymph nodes of Thy 1.2 (AKR-Cu) mice. Lymph node localization of anti-Thy 1.1-liposomes was equal to that of control monoclonal antibody-liposomes in Thy 1.2 mice. Conjugation to either monoclonal antibody substantially increased liposome clearance by the liver, while decreasing liposome uptake in a number of organs outside the reticuloendothelial system. Changes in liposome size and phospholipid composition did not significantly alter these results. Administration of a large predose of unconjugated liposomes prior to injection of MRCOX7-conjugated liposomes increased blood levels and reduced liver uptake of the monoclonal antibody-**liposome conjugates**, but did not further enhance lymph node uptake. This study demonstrates that targeting of liposomes by conjugation to the appropriate monoclonal antibody, can significantly increase their uptake in lymph nodes which contain high levels of cells expressing the target antigen. However, conjugation to monoclonal antibody also increases clearance of liposomes by the liver. To increase the uptake of monoclonal antibody-conjugated liposomes in target tissue, substantial reduction of their clearance by the reticuloendothelial system will be required.

L16 ANSWER 157 OF 179 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
1986:325893 Document No.: PREV198631040475; BR31:40475. **LIPOSOME CONJUGATES** WITH DIAGNOSTIC METHODS THEREWITH US PATENT-4598051. JULY 1 1986. PAPAHADJOPOULOS D P [Inventor, Reprint author]; HEATH T D [Inventor]. LAFAYETTE, CALIF, USA ASSIGNEE THE REGENTS OF THE UNIVERSITY OF CALIFORNIA. ASSIGNEE: THE REGENTS OF THE UNIVERSITY OF CALIFORNIA. Patent Info.: US 4598051 July 01, 1986. Official Gazette of the United States Patent and Trademark Office Patents, (1986) Vol. 1068, No. 1, pp. 325.
CODEN: OGUPE7. ISSN: 0098-1133. Language: ENGLISH.

L16 ANSWER 158 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1986:184783 Document No. 104:184783 Production of immunogens by antigen conjugation to liposomes. Heath, Timothy D.; Shek, Pang; Papahadjopoulos, Demetrios (University of California, USA). U.S. US 4565696 A 19860121, 5 pp. (English). CODEN: USXXAM. APPLICATION: US 1983-520090 19830803.
AB A method for potentiating an immune response is provided whereby immunogens are covalently linked to liposome above a min. ratio of immunogen to lipid to optimize the immune response. In general, the liposome are prepared from various lipids including phosphatidyl ethers and esters and have active functional groups, preferably activated olefins. The immunogens or antigens are primarily poly(amino acids) including peptides and proteins. The antigen may be joined to the liposome in an appropriate ratio under conditions where covalent bonds are found between the vesicle and the antigen. Preferably, ≥25 g protein/mol lipid (most prefered ≥40g protein/mol lipid) are required. It is of particular importance to utilize an immunomodulator (e.g. various drugs, bacterial isolates) in the aqueous space or in the bilayer of the vesicle-antigen **conjugate.** These **conjugates** may be administered through a vertebrate host in conventional ways and used for the production of monoclonal or polyclonal antibodies. In some cases, the vesicle-protein **conjugates** may be combined with peripheral blood

cells, or transformed β-lymphocytes to produce antibodies.

L16 ANSWER 159 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1987:470805 Document No. 107:70805 Compositions and process for protecting T-lymphocytes against the etiological agent of lymphadenopathy and an acquired immunodepression syndrome. Klatzmann, David; Gluckman, Jean Claude; Montagnier, Luc (Institut Pasteur, Fr.; Centre National de la Recherche Scientifique; Universite Pierre et Marie Curie Paris VI). Eur. Pat. Appl. EP 176429 A1 19860402, 13 pp. DESIGNATED STATES: R: AT, BE, CH, DE, GB, IT, LI, LU, NL, SE. (French). CODEN: EPXXDW. APPLICATION: EP 1985-401780 19850913. PRIORITY: FR 1984-14172 19840914.
AB The title compns. and process comprise an antibody to T-lymphocyte protein T4 or the protein itself which appears to be the principal target of the human T-cell leukemia type III virus (HTLV-III). The antibody is free or covalently coupled to an antiviral substance such as an antibody against HTLV-III, particularly the viral envelope, or the antibody is conjugated with liposomes containing an antiviral substance. Lymphocytes susceptible to infection by the virus are contacted with the antibody or analog. The virus, and if necessary, the anti-T4 antibody resulting from an autoimmune mechanism, can be removed from serum of lymphadenopathy or AIDS patients by passing the plasma through an affinity column containing T4 mols. Infected lymphocytes can be removed by passing the plasma through an affinity column containing anti-T4 antibodies.

L16 ANSWER 160 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1987:162462 Document No. 106:162462 Antitumor effect of adriamycin entrapped in liposomes conjugated with monoclonal antibody against tumor-associated antigen of bovine leukemia cells. Onuma, Misao; Odawara, Terukazu; Watarai, Shinobu; Aida, Yoko; Ochiai, Kenji; Syuto, Bunei; Matsumoto, Kozo; Yasuda, Tatsuji; Fujimoto, Yutaka; et al. (Dep. Vet. Microbiol., Coll. Dairy Agric., Ebetsu, 069, Japan). Japanese Journal of Cancer Research, 77(11), 1161-7 (English) 1986. CODEN: JJCREP. ISSN: 0910-5050.
AB Monoclonal antibody against tumor-associated antigen (TAA) expressed on bovine leukemia cells was conjugated to liposomes containing adriamycin (ADM) [23214-92-8], and the specificity and therapeutic effects of the **conjugates** were examined in vitro and in vivo using a TAA-pos. bovine leukemia cell line as the target tumor. In vitro studies with the TAA-pos. cell line clearly indicated that the antibody-conjugated liposomes containing ADM exerted selective effects on TAA-pos. cells in the inhibition assay of 3H-thymidine incorporation. Three injections of liposomes containing ADM (4 mg/kg) into tumor-bearing nude mice significantly inhibited the tumor growth and the therapeutic effect of the antibody-conjugated liposomes was far greater than that of normal mouse IgG-conjugated liposomes as assessed in terms of tumor size.

L16 ANSWER 161 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1987:546911 Document No. 107:146911 Cytotoxic activity of monoclonal antibody (KOR-N34)-liposome-adriamycin **conjugates** to cultured lymphoid cell lines. Nishino, Kazuyoshi; Nakazawa, Shinpei; Mori, Taijiro; Sugita, Kanji; Abe, Takashi; Suzuki, Toshio; Kinoshita, Akitoshi; Osano, Mitsuru; Tadakuma, Takushi; et al. (Sch. Med., Keio Univ., Tokyo, Japan). Nippon Gan Chiryo Gakkaishi, 21(5), 1016-25 (Japanese) 1986. CODEN: NGCJAK. ISSN: 0021-4671.
AB Monoclonal antibodies (KOR-N34) to common ALL antigen (CALLA) were conjugated with adriamycin (ADM) entrapped in liposomes by using the heterobifunctional cross-linking reagent N-hydroxysuccinimidyl 3-(2-pyridyldithio)propionate. In human leukemia cell lines, the monoclonal antibody-liposome-adriamycin **conjugates** had marked cytotoxicity to ADM-sensitive NALM-6 cells with pos. CALLA, but did not affect the growth of CALLA-neg. cell lines and ADM-resistant cell lines, suggesting that monoclonal antibodies conjugated with antileukemic agents might have important therapeutic potentials.

L16 ANSWER 162 OF 179 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 39

1987:186637 Document No.: PREV198783094761; BA83:94761. CONCANAVALIN A IMMOBILIZED ON THE SURFACE OF LIPOSOMES DIFFERENCES IN ITS BINDING TO NORMAL AND TRANSFORMED MOUSE FIBROBLASTS. BOGDANOV A A [Reprint author]; GORDEEVA L V; MARGOLIS L B; TORCHILIN V P. INST EXP CARDIOL, ALL-UNION CARDIOL SCI CENT, ACAD MED SCI USSR, MOSCOW, USSR. Biologicheskie Membrany ,(Moscow), (1986) Vol. 3, No. 7, pp. 674-684.
CODEN: BIMEE9. ISSN: 0233-4755. Language: RUSSIAN.

AB The **conjugates** of small unilamellar liposomes and concanavalin A were obtained. A microfluorimetric study on the **conjugate** binding to mouse fibroplasts revealed that 70% of the total binding was accounted for by specific interaction of concanavalin A with the cell surface receptors. A different binding of the concanavalin A-**liposome conjugates** to mouse fibroplast of the normal and transformed cell lines was observed, the transformed cells binding 2 ÷ 2.5 times more **conjugates** than the normal ones. Brief trypsinization of the normal fibroplasts produced a substantial increase in the **conjugate** binding. A model system "cell-lectin bound liposomes" was proposed for investigating the lectin-mediated cell agglutination.

L16 ANSWER 163 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

1986:558670 Document No. 105:158670 The development and application of protein-liposome conjugation techniques. Heath, Timothy D.; Martin, Francis J. (Sch. Pharm., Univ. Wisconsin, Madison, WI, 53706, USA). Chemistry and Physics of Lipids, 40(2-4), 347-58 (English) 1986. CODEN: CPLIA4. ISSN: 0009-3084.

AB A review with 55 refs. on coupling of proteins to liposomes for drug targeting. Characteristics of protein-**liposome conjugates** are discussed.

L16 ANSWER 164 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

1987:38307 Document No. 106:38307 Antitumor effect of adriamycin entrapped in liposomes conjugated with anti-human α-fetoprotein monoclonal antibody. Konno, H.; Tadakuma, T.; Kumai, K.; Suzuki, H.; Takahashi, T.; Yasuda, T.; Kubota, T.; Nagaike, K.; Muramatsu, M.; et al. (Dep. Surg., Keio Univ., Tokyo, Japan). Recent Adv. Chemother., Proc. Int. Congr. Chemother., 14th, Volume Anticancer Sect. 1, 405-6. Editor(s): Ishigami, Joji. Univ. Tokyo Press: Tokyo, Japan. (English) 1985. CODEN: 55GNAX.

AB Monoclonal antibodies against human α-fetoprotein(AFP) [MoAb(AFP)] adriamycin (ADM) [23214-92-8]. The selective binding of the MoAb(AFP) conjugated liposomes to AFP pos. tumor cells was demonstrated using fluoroscent liposomes. In vitro studies clearly indicated that MoAb(AFP) conjugated liposomes containing ADM exerted the effects selectivity on AFP pos. cells. Three shots of liposomes containing ADM(7.5mg/kg) into the tumor bearing mice significantly inhibited the tumor growth and the therapeutic effect of the MoAb(AFP) conjugated liposomes was far greater than that of uncinjugated liposomes as assessed by tumor weight and histol. findings.

L16 ANSWER 165 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

1985:594628 Document No. 103:194628 A simple procedure to elicit sugar specific antibodies using liposomes. Sarkar, Debi Prasad; Das, Manoji K. (Dep. Enzyme Eng., Indian Inst. Chem. Biol., Calcutta, 700 032, India). Indian Journal of Biochemistry & Biophysics, 22(4), 244-6 (English) 1985. CODEN: IJBBBQ. ISSN: 0301-1208.

AB N-ε-Aminocaproyl-β-D-galactopyranosylamine was coupled to phosphatidylethanolamine-containing liposomes by glutaraldehyde. The galactosylated liposomes, when injected into rabbits in saline, elicited an immune response specific for D-galactose. This method should prove useful in raising antisera specific for other saccharide haptens or polysaccharide antigens without employing Freund's adjuvant.

L16 ANSWER 166 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN

1985:613053 Document No. 103:213053 Equilibrium and kinetic parameters for the interaction of IgG and Fab with haptenated liposomes. Petrossian, Ashot (Univ. California, Berkeley, CA, USA). 218 pp. Avail. Univ.

Microfilms Int., Order No. DA8512958 From: Diss. Abstr. Int. B 1985, 46(4), 1036 (English) 1984.
AB Unavailable

L16 ANSWER 167 OF 179 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
84218785 EMBASE Document No.: 1984218785. Use of heterobifunctional cross-linking reagents to prepare antibody-**liposome conjugates**: Development of methods to reduce liposome aggregation during conjugation. Jou Y.-H.; Jarlinksi S.; Mayhew E.; Bankert R.B.. Abbott Diagnostic Div., Abbott Laboratories, N. Chicago, IL 60064, United States. Federation Proceedings 43/7 (no. 3218) 1984.
CODEN: FEPRA7. Pub. Country: United States. Language: English.

L16 ANSWER 168 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1984:443439 Document No. 101:43439 Antibodies to hepatitis B surface antigen (HBsAg) elicited by immunization with a synthetic peptide covalently linked to liposomes. Neurath, A. R.; Kent, S. B. H.; Strick, N. (Lindsley F. Kimball Res. Inst., New York Blood Cent., New York, NY, 10021, USA). Journal of General Virology, 65(5), 1009-14 (English) 1984. CODEN: JGVIAY. ISSN: 0022-1317.
AB A synthetic peptide corresponding to residues 135-155 (P135-155) of HBsAg failed to elicit in free form antipeptide antibodies or anti-HBs. However, polymers of P135-155 (prepared by linking to diaminoalkanes) and synthetic **conjugates** prepared by binding P135-155 to liposomes or polylysine were immunogenic. A poor correlation was observed between anti-peptide and anti-HBs responses elicited by these **conjugates**. Glutaraldehyde-fixed liposomes appeared to be the carriers of choice for inducing anti-HBs.

L16 ANSWER 169 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1985:191064 Document No. 102:191064 Increased circulatory half-life of liposomes after conjunction with dextran. Pain, D.; Das, P. K.; Ghosh, P.; Bachhawat, B. K. (Indian Inst. Chem. Biol., Calcutta, 700 032, India). Journal of Biosciences (Bangalore, India), 6(6), 811-16 (English) 1984. CODEN: JOBSDN. ISSN: 0250-5991.
AB Dextran was covalently coupled to neutral unilammelar liposomes. Dextran conjugated liposomes were cleared from the circulation at a much slower rate than unconjugated liposomes. The uptake of dextran conjugated liposomes by liver and spleen was also decreased. The amount of dextran on the surface of liposomes was a determining factor for their stability in circulation. Dextran conjugated liposomes therefore may be a more effective way of controlled drug release.

L16 ANSWER 170 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1984:437024 Document No. 101:37024 Characterization of anti-N-acetyl-D-glucosamine antibodies elicited through haptenated liposomes. Das, Manoj K.; Roy, Samir K.; Sarkar, Debi Prasad (Dep. Enzyme Eng., Indian Inst. Chem. Biol., Calcutta, 700 032, India). Carbohydrate Research, 128(2), 335-40 (English) 1984. CODEN: CRBRAT. ISSN: 0008-6215.
AB Antiserum was raised in rabbits against p-aminophenyl 2-acetamido-2-deoxy-β-D-glucoside covalently coupled to phosphatidylaminoethanol-containing lecithin liposomes. The affinity-purified antibodies were IgM. The properties of the antibodies were studied by ligand inhibition of quant. precipitation, fluorescence titration with 2-acetamido-2-deoxy-D-glucose, and complement lysis of haptenated liposomes.

L16 ANSWER 171 OF 179 MEDLINE on STN DUPLICATE 40
85170520. PubMed ID: 6532005. Antibody response to two synthetic peptides corresponding to residues 45-68 and 69-79 of the major protein of hepatitis B surface antigen. Neurath A R; Kent S B; Strick N. Virus research, (1984) 1 (4) 321-31. Journal code: 8410979. ISSN: 0168-1702. Pub. country: Netherlands. Language: English.
AB Peptides corresponding to amino acid residues 48-65 and 69-79 of the major polypeptide component of hepatitis B surface antigen (HBsAg) were

synthesized and conjugated to protein (bovine serum albumin and keyhole limpet hemocyanin) and fully synthetic (polyglutaraldehyde and cross-linked liposomes) carriers. The peptide-**liposome conjugates** appeared the most consistent in eliciting antibodies to HBsAg. Results of competition assays between each of the free synthetic peptides and HBsAg for antibodies suggested that the synthetic analogues and the corresponding segments on intact HBsAg are structurally closely related.

L16 ANSWER 172 OF 179 MEDLINE on STN DUPLICATE 41
84203612. PubMed ID: 6547057. Immunologic response to protein immobilized on the surface of liposomes via covalent azo-bonding. Snyder S L; Vannier W E. Biochimica et biophysica acta, (1984 May 30) 772 (3) 288-94. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB A new method for immobilizing protein on the surface of liposomes is described. Inclusion of N-(p-aminophenyl) stearylamide in the lipid composition of vesicles resulted in liposomes that could be 'activated' by diazotization with NaNO2/HCl, and subsequently coupled with protein. Using this method 39.7 +/- 7.5 micrograms egg albumin/mumol phospholipid has been coupled to multilamellar vesicles composed of phosphatidylcholine, cholesterol, and N-(p-aminophenyl) stearylamide in a molar ratio of 15:75:1.1. Furthermore, when the immunologic response of mice to egg albumin that was encapsulated in, nonspecifically absorbed, or covalently linked to liposomes was investigated, only the covalent protein-**liposome conjugates** elicited pronounced and sustained elevations in antibody titers. These results suggest that the immunoadjuvant effects of liposomes can be maximized by covalently linking protein antigens to their surface.

L16 ANSWER 173 OF 179 MEDLINE on STN DUPLICATE 42
85081403. PubMed ID: 6549019. Lectin-mediated binding of liposome-inserted membrane proteins to red blood cells. A method to detect binding of antibodies to purified rat histocompatibility antigen or binding of insulin to the insulin receptor. Eriksson H; Mattiasson B; Sjogren H O. Journal of immunological methods, (1984 Dec 14) 75 (1) 167-79. Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB Partially purified membrane proteins such as the rat RT-1 histocompatibility antigen or the insulin receptor of porcine liver were inserted into liposomes. These liposomes then bound efficiently to Con A-coated red blood cells. After attachment of the liposomes to the cells, cell-**liposome conjugates** could be separated from free liposomes by centrifugation. Binding of FITC-labeled specific antibodies or insulin to membrane proteins inserted into the liposomes could then be analyzed with a cell flow cytofluorometer. The amount of RT-1 antigen that became associated with the cells depended on the composition and concentration of phospholipids during liposome formation. No association of RT-1 antigen to the cells was obtained in the presence of 50 mM alpha-methyl mannoside. The technique allows detection of micrograms amounts of the histocompatibility antigen associated with the red blood cells. It was possible to detect binding of insulin to cells to which approximately 9 ng (3 X 10(-14) mol) insulin receptor/10(6) cells had been attached. This amount of membrane protein was close to the detection limit of the method.

L16 ANSWER 174 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1984:137110 Document No. 100:137110 Antibody-directed liposomes. Determination of affinity constants for soluble and liposome-bound antifluorescein. Heath, T. D.; Fraley, R. T.; Bentz, J.; Voss, E. W., Jr.; Herron, J. N.; Papahadjopoulos, D. (Cancer Res. Inst., Univ. California, San Francisco, CA, 94143, USA). Biochimica et Biophysica Acta, 770(2), 148-58 (English) 1984. CODEN: BBACAQ. ISSN: 0006-3002.

AB The binding of liposomes conjugated with antifluorescein antibody specific for fluorescein isothiocyanate-modified erythrocytes was used as a model

for multivalent antigen-antibody interactions. A series of liposome prepns. which were conjugated to between 0 and 332 active antibodies/liposome were examined The antigen-binding capacity and mean intrinsic affinity of the soluble and conjugated antibody were determined by fluorescence quenching of carboxyfluorescein. Liposome-cell interaction data was fitted with a Scatchard-type equation. Functional affinity of liposomes for cells was ≤1000-fold greater than the intrinsic affinity of the antibody for soluble ligand. Anal. for binding at high cell concns. revealed that liposome-induced cell agglutination reduces the number of available binding sites per cell.

L16 ANSWER 175 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1983:468764 Document No. 99:68764 **Liposome conjugates** and diagnostic methods. Papahadjopoulos, Demetrious P.; Heath, Timothy D. (University of California, USA). PCT Int. Appl. WO 8301571 A1 19830511, 42 pp. DESIGNATED STATES: W: JP; RW: AT, BE, CH, DE, FR, GB, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1982-US1524 19821028. PRIORITY: US 1981-316126 19811029.

AB A method is described for producing liposome-antibody **conjugates** to provide a rapid and sensitive method having an improved capacity to agglutinate erythrocytes (in comparison to using soluble antibody), and for use especially in blood typing and other hemagglutination assays. Ligand antibodies can include various normal human and animal Igs and Ig fractions and antibodies specific for erythrocyte and T cell antigens. For example, for blood typing, liposomes (0.5 μm) (activated by peroxide) are covalently bound to antibody (40 μg antibody/μmol lipid), and the liposome protein **conjugates** are separated from unbound antibody by flotation in a discontinuous metriazamide gradient. The min. hemagglutination concentration of the **conjugates** is determined, and then the **conjugates** are mixed with the test erythrocytes.

L16 ANSWER 176 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1983:436820 Document No. 99:36820 A method of introducing lipid-conjugated antigens into the surface of schistosomula. Levi-Schaffer, Francesca; Schryer, Michelle D.; Tarrab-Hazdai, Rebeca; Smolarsky, Moshe (Dep. Chem. Immunol., Weizmann Inst. Sci., Rehovot, Israel). American Journal of Tropical Medicine and Hygiene, 32(2), 343-9 (English) 1983. CODEN: AJTHAB. ISSN: 0002-9637.

AB Introduction of synthetic antigens into the surface of schistosomula of Schistosoma mansoni was achieved by brief incubation of the worms with liposomes carrying the lipid-bound antigens in their bilayers. Three-hour-old schistosomula were surface-labeled with lipid-conjugated dinitrophenyl (DNP) groups by using liposomes made of egg lecithin-N-dinitrophenil-ε-aminocaproyl-phosphatidylethanolamine (5:1). The DNP groups incorporated in this way could be detected for more than 21 h in vitro by using rabbit anti-DNP antibodies stained with fluorescein isothiocyanate-conjugated goat antirabbit IgG. Immunofluorescence microscopy showed the lipid antigen to be uniformly distributed over the entire surface of the worms. Electron microscope studies, performed with purified rabbit anti-DNP antibodies followed by ferritin-conjugated goat antirabbit IgG, showed that the DNP groups were evenly and densely distributed over the entire outer membrane of the schistosomula, including spines. The distance between the ferritin mols. and the parasite's surface was 24 nm, indicating that the lipid antigen had been incorporated into the outer membrane of the schistosomula.

L16 ANSWER 177 OF 179 MEDLINE on STN DUPLICATE 43
83289419. PubMed ID: 6193054. Immune response mediated by liposome-associated protein antigens. III. Immunogenicity of bovine serum albumin covalently coupled to vesicle surface. Shek P N; Heath T D. Immunology, (1983 Sep) 50 (1) 101-6. Journal code: 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.

AB A protein antigen, bovine serum albumin (BSA), was covalently linked to the surface of preformed large unilamellar vesicles composed of phosphatidylcholine, cholesterol, and N-[4-(p-

maleimidophenyl)butyryl]phosphatidylethanolamine (MPB-PE). The interaction between thiolated BSA and MPB-PE resulted in the production of a protein-**liposome conjugate** via the formation of an irreversible covalent bond. Mice immunized with liposome-coupled BSA were found to generate a vigorous BSA-specific plaque-forming cell (PFC) response. No significant response was observed in control animals given simultaneous, but separate injections of thiol-BSA and liposomes. Thus, there seems to be a need for successful and stable linkage between the antigen and the carrier. The elicitation of an optimal antigen-specific PFC response was also found to require the vesicle surface to be coated with a certain minimum distribution of the antigen. Results of this study demonstrate that the covalent coupling of a protein antigen to the liposome surface is very effective in potentiating the protein-specific antibody response and the immunogenicity of the **conjugate** is dependent on the epitope density of the antigen.

L16 ANSWER 178 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1982:613937 Document No. 97:213937 The adjuvant effect of liposomes in eliciting antigalactosyl antibodies. Sarkar, Debi Prasad; Das, Pijush K.; Bachhawat, Bimal K.; Das, Manoj K. (Dep. Enzyme Eng., Indian Inst. Chem. Biol., Calcutta, India). Immunological Communications, 11(3), 175-88 (English) 1982. CODEN: IMLCAV. ISSN: 0090-0877.
AB Neg.-charged, multilamellar liposomes, covalently coupled with p-aminophenyl-β-D-galactopyranoside, elicited in rabbits a nearly equivalent anti-galactosyl immune response in both the presence and the absence of complete Freund's-adjuvant (CFA). The antibody response obtained using liposomes both as the carrier and adjuvant was better than that obtained through the conventional method of using a protein carrier in CFA.

L16 ANSWER 179 OF 179 CAPLUS COPYRIGHT 2004 ACS on STN
1982:470534 Document No. 97:70534 Liposomes as carriers for production of sugar specific antibodies: preparation of antigalactosyl antiserum. Das, Pijush K.; Ghosh, Prahlad; Bachhawat, Bimal K.; Das, Manoj K. (Dep. Enzyme Eng., Indian Inst. Chem. Biol., Calcutta, India). Immunological Communications, 11(1), 17-24 (English) 1982. CODEN: IMLCAV. ISSN: 0090-0877.
AB Neg. charged multilamellar liposomes, covalently coupled with a p-aminophenylated derivative of D-galactose, were used to raise galactose-specific antibodies in rabbits. The specificity of the antiserum was characterized by immunodiffusion, quant. precipitation, and hapten inhibition studies. In addition to its specificity against the sugar moiety, the antibody population also recognizes the aromatic aglycone portion of the introduced hapten. This offers a new method of raising sugar-specific antibodies using liposomes, instead of proteins, as immunol. carriers.

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=> s diacylphosphatidylcholine and diacyphosphatidyglycerol
L18           0 DIACYLPHOSPHATIDYLCHOLINE AND DIACYPHOSPHATIDYGLYCEROL

=> s (bergeron m?/au or desormeaux a?/au or tremblay m?/au)
L19        4159 (BERGERON M?/AU OR DESORMEAUX A?/AU OR TREMBLAY M?/AU)

=> s l19 and liposome conjugate
L20           0 L19 AND LIPOSOME CONJUGATE

=> s l19 and HIV
L21         540 L19 AND HIV

=> s l21 and targeting
L22          38 L21 AND TARGETING

=> dup remove l22
PROCESSING COMPLETED FOR L22
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L23 16 DUP REMOVE L22 (22 DUPLICATES REMOVED)

=> d 'l23 1-16 cbib abs

L23 ANSWER 1 OF 16 MEDLINE on STN DUPLICATE 1

2002625818. PubMed ID: 12384349. The immunosuppressant rapamycin represses human immunodeficiency virus type 1 replication. Roy Jocelyn; Paquette Jean-Sebastien; Fortin Jean-Francois; **Tremblay Michel J.** (Centre de Recherche en Infectiologie, Hopital CHUL, Centre Hospitalier Universitaire de Quebec, and Departement de Biologie Medicale, Faculte de Medecine, Universite Laval, Ste-Foy, Quebec, Canada G1V 4G2.) Antimicrobial agents and chemotherapy, (2002 Nov) 46 (11) 3447-55. Journal code: 0315061. ISSN: 0066-4804. Pub. country: United States. Language: English.

AB The immunosuppressive macrolide rapamycin is used in humans to prevent graft rejection. This drug acts by selectively repressing the translation of proteins that are encoded by an mRNA bearing a 5'-polypyrimidine tract (e.g., ribosomal proteins, elongation factors). The human immunodeficiency virus type 1 (**HIV**-1) carries a polypyrimidine motif that is located within the tat exon 2. Treatment of human T lymphoid cells with rapamycin resulted in a marked diminution of **HIV**-1 transcription when infection was performed with luciferase reporter T-tropic and macrophage-tropic viruses. Replication of fully infectious **HIV**-1 particles was abolished by rapamycin treatment. The rapamycin-mediated inhibitory effect on **HIV**-1 production was reversed by FK506. The anti-**HIV**-1 effect of rapamycin was also seen in primary human cells (i.e., peripheral blood lymphocytes) from different healthy donors. Rapamycin was shown to diminish basal **HIV**-1 long terminal repeat gene expression, and the observed effect of rapamycin on **HIV**-1 replication seems to be independent of the virus-specific transactivating Tat protein. A constitutive beta-actin promoter-based reporter gene vector was unaffected by rapamycin treatment. Kinetic virus infection studies and exposure to reporter viruses pseudotyped with heterologous envelope proteins (i.e., amphotropic murine leukemia virus and vesicular stomatitis virus G) suggested that rapamycin is primarily affecting the life cycle of **HIV**-1 at a transcriptional level. Northern blot analysis confirmed that this compound is selectively **targeting HIV**-1 mRNA synthesis.

L23 ANSWER 2 OF 16 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 2

2002034261 EMBASE Targeted delivery of indinavir to **HIV**-1 primary reservoirs with immunoliposomes. Gagne J.-F.; **Desormeaux A.**; Perron S.; **Tremblay M.J.**; **Bergeron M.G.**. M.G. Bergeron, Centre de Recherche en Infectiologie, Centre Hospitalier Univ. de Quebec, Universite Laval, 2705 Blvd Laurier, Quebec, Que., Canada. michel.g.bergeron@crchul.ulaval.ca. Biochimica et Biophysica Acta - Biomembranes 1558/2 (198-210) 1 Feb 2002. Refs: 44. ISSN: 0005-2736. CODEN: BBBMBS. Publisher Ident.: S 0005-2736(01)00432-1. Pub. Country: Netherlands. Language: English. Summary Language: English.

AB The tissue distribution of indinavir, free or incorporated into sterically stabilized anti-HLA-DR immunoliposomes, has been evaluated after a single subcutaneous injection to C3H mice. Administration of free indinavir resulted in low drug levels in lymphoid organs. In contrast, sterically stabilized anti-HLA-DR immunoliposomes were very efficient in delivering high concentrations of indinavir to lymphoid tissues for at least 15 days post-injection increasing by up to 126 times the drug accumulation in lymph nodes. The efficacy of free and immunoliposomal indinavir has been evaluated in vitro. Results showed that immunoliposomal indinavir was as efficient as the free agent to inhibit **HIV**-1 replication in cultured cells. The toxicity and immunogenicity of repeated administrations of liposomal formulations have also been investigated in

rodents. No significant differences in the levels of hepatic enzymes of mice treated with free or liposomal indinavir were observed when compared to baseline and control untreated mice. Furthermore, histopathological studies revealed no significant damage to liver and spleen when compared to the control group. Liposomes bearing Fab' fragments were 2.3-fold less immunogenic than liposomes bearing the entire IgG. Incorporation of antiviral agents into sterically stabilized immunoliposomes could represent a novel therapeutic strategy to target specifically **HIV** reservoirs and treat more efficiently this retroviral infection.

L23 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
2000:790356 Document No. 133:340273 Methods and formulations for **targeting** infectious agents bearing host cell proteins. **Bergeron, Michel G.; Desormeaux, Andre; Tremblay, Michel J.** (Infectio Recherche Inc., Can.). PCT Int. Appl. WO 2000066173 A2 20001109, 45 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-CA469 20000503. PRIORITY: CA 1999-2270600 19990503.
AB A formulation is disclosed for the treatment of diseases caused by an infectious agent which acquires host membranes protein during its life cycle. The formulation is a **targeting** pharmaceutical composition It comprises a ligand capable of binding the host membrane proteins coupled to a lipid-comprising vesicle, which may comprise or not a drug effective in the treatment of the disease. Specific liposomes bearing anti-HLA-DR or anti-CD4 antibodies comprising or not antiviral drugs, namely anti-**HIV** drugs, are disclosed and claimed. A method of formulation as well as a method of using the formulation in the treatment of a disease are also disclosed.

L23 ANSWER 4 OF 16 MEDLINE on STN DUPLICATE 3
2001338262. PubMed ID: 11101055. **Targeting** cell-free **HIV** and virally-infected cells with anti-HLA-DR immunoliposomes containing amphotericin B. Bestman-Smith J; **Desormeaux A; Tremblay M J; Bergeron M G.** (Centre de Recherche en Infectiologie, Centre Hospitalier Universitaire de Quebec, Canada.) AIDS (London, England), (2000 Nov 10) 14 (16) 2457-65. Journal code: 8710219. ISSN: 0269-9370. Pub. country: ENGLAND: United Kingdom. Language: English.
AB OBJECTIVE: To evaluate the ability of liposomes bearing anti-HLA-DR Fab' fragments (immunoliposomes) and containing amphotericin B (AmB) to target and neutralize cell-free **HIV**-1 particles and virally-infected cells. METHODS: The effect of AmB on the attachment and fusion of **HIV**-1(NL4-3) to Jurkat E6.1 cells has been evaluated using a p24 enzymatic assay. The ability of AmB to inhibit **HIV**-1-based luciferase reporter viruses pseudotyped with HXB2, AML-V and VSV-G envelopes has been evaluated in Jurkat E6.1 cells. The efficacy of free and immunoliposomal AmB to inhibit cell-free **HIV**, that have incorporated or not HLA-DR molecules, has been evaluated in HLA-DR/negative (NEG) 1G5 T cells and HLA-DR/positive (POS) Mono Mac 1 cells. RESULTS: AmB inhibited **HIV** infectivity independently of the nature of viral envelope proteins. Pretreatment of **HIV** with AmB had no major effect on viral attachment and fusion process to Jurkat E6.1 cells. Immunoliposomal AmB (0.5 microg/ml) led to a 77% inhibition of replication of HLA-DR/POS **HIV**-1 with no cell toxicity, whereas free AmB had no significant antiviral activity at this concentration. A complete inhibition of viral replication was observed following incubation of viruses with immunoliposomal AmB (2.5 microg/ml). Anti-HLA-DR immunoliposomes containing AmB had no effect on the infectivity of HLA-DR/NEG **HIV**-1 particles in HLA-DR/NEG T

lymphoid cells but completely inhibited replication of viruses in an HLA-DR/POS monocytic cell line. CONCLUSION: The incorporation of neutralizing agents in anti-HLA-DR immunoliposomes could represent a novel therapeutic strategy to specifically target cell-free **HIV** particles and virally-infected cells to treat **HIV** infection more efficiently.

L23 ANSWER 5 OF 16 MEDLINE on STN DUPLICATE 4

2001048034. PubMed ID: 11018661. Sterically stabilized liposomes bearing anti-HLA-DR antibodies for **targeting** the primary cellular reservoirs of **HIV**-1. Bestman-Smith J; Gourde P; **Desormeaux A; Tremblay M J; Bergeron M G.** (Centre de Recherche en Infectiologie, Centre Hospitalier Universitaire de Quebec, Pavillon CHUL, 2705 Blvd Laurier, G1V 4G2, Quebec, QC, Canada.) Biochimica et biophysica acta, (2000 Sep 29) 1468 (1-2) 161-74. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB The ability of liposomes bearing anti-HLA-DR Fab' fragments at the end termini of polyethyleneglycol chains (sterically stabilized immunoliposomes) to target HLA-DR expressing cells and increase the accumulation of liposomes into lymphoid organs has been evaluated and compared to that of conventional liposomes, sterically stabilized liposomes and conventional immunoliposomes after a single subcutaneous injection to mice. The accumulation of sterically stabilized liposomes in lymph nodes was higher than that of conventional liposomes. Sterically stabilized immunoliposomes accumulated much better than conventional immunoliposomes in all tissues indicating that the presence of PEG has an important effect on the uptake of immunoliposomes by the lymphatic system. Fluorescence microscopy studies showed that sterically stabilized liposomes are mainly localized in macrophage-rich areas such as the subcapsular region of lymph nodes and in the red pulp and marginal zone of the spleen. In contrast, sterically stabilized immunoliposomes mostly accumulated in the cortex in which follicles are located and in the white pulp of the spleen. As the human HLA-DR determinant of the major histocompatibility complex class II is expressed on activated CD4+ T lymphocytes and antigen presenting cells such as monocyte/macrophages and dendritic cells, known as the cellular reservoirs of **HIV**-1, liposomes bearing anti-HLA-DR antibodies constitute an attractive approach to concentrate drugs in **HIV**-1 reservoirs and improve their therapeutic effect.

L23 ANSWER 6 OF 16 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

2000:781660 The Genuine Article (R) Number: 363CF. Sterically stabilized liposomes bearing anti-HLA-DR antibodies for **targeting** the primary cellular reservoirs of **HIV**-1. BestmanSmith J; Gourde P; **Desormeaux A; Tremblay M J; Bergeron M G (Reprint).** CHU QUEBEC, CTR RECH INFECT, PAVILLON CHUL, 2705 BLVD LAURIER, QUEBEC CITY, PQ G1V 4G2, CANADA (Reprint); CHU QUEBEC, CTR RECH INFECT, QUEBEC CITY, PQ G1V 4G2, CANADA. BIOCHIMICA ET BIOPHYSICA ACTA-BIOMEMBRANES (29 SEP 2000) Vol. 1468, No. 1-2, pp. 161-174. Publisher: ELSEVIER SCIENCE BV. PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS . ISSN: 0005-2736. Pub. country: CANADA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The ability of liposomes bearing anti-HLA-DR Fab' fragments at the end termini of polyethyleneglycol chains (sterically stabilized immunoliposomes) to target HLA-DR expressing cells and increase the accumulation of liposomes into lymphoid organs has been evaluated and compared to that of conventional liposomes, sterically stabilized liposomes and conventional immunoliposomes after a single subcutaneous injection to mice. The accumulation of sterically stabilized liposomes in lymph nodes was higher than that of conventional liposomes. Sterically stabilized immunoliposomes accumulated much better than conventional immunoliposomes in all tissues indicating that the presence of PEC has an important effect on the uptake of immunoliposomes by the lymphatic system. Fluorescence microscopy studies showed that sterically stabilized

liposomes are mainly localized in macrophage-rich areas such as the subcapsular region of lymph nodes and in the red pulp and marginal zone of the spleen. In contrast, sterically stabilized immunoliposomes mostly accumulated in the cortex in which follicles are located and in the white pulp of the spleen. As the human HLA-DR determinant of the major histocompatibility complex class II is expressed on activated CD4+ T lymphocytes and antigen presenting cells such as monocyte/macrophages and dendritic cells, known as the cellular reservoirs of **HIV**-1, liposomes bearing anti-HLA-DR antibodies constitute an attractive approach to concentrate drugs in **HIV**-1 reservoirs and improve their therapeutic effect. (C) 2000 Elsevier Science B.V. All rights reserved.

L23 ANSWER 7 OF 16 MEDLINE on STN DUPLICATE 5
2000001973. PubMed ID: 10518698. **Targeting** lymph nodes with liposomes bearing anti-HLA-DR Fab' fragments. Dufresne I; **Desormeaux A**; Bestman-Smith J; Gourde P; **Tremblay M J**; **Bergeron M G.** (Centre de Recherche en Infectiologie, Universite Laval, Centre Hospitalier Universitaire de Quebec, Pavillon CHUL, 2705 Blvd. Laurier, Quebec, QC, Canada.) Biochimica et biophysica acta, (1999 Oct 15) 1421 (2) 284-94. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB The ability of liposomes bearing anti-HLA-DR Fab' fragments to target cells expressing the human HLA-DR determinant of the major histocompatibility complex class II (MHC-II) has been evaluated and compared to that of conventional liposomes. Anti-HLA-DR immunoliposomes did not bind to HLA-DR-negative cells. In contrast, a high level of binding was observed following incubation of immunoliposomes with cells bearing important levels of human HLA-DR. The accumulation of conventional and murine anti-HLA-DR immunoliposomes in different tissues has been investigated following a single subcutaneous injection given in the upper back of C3H mice. Anti-HLA-DR immunoliposomes resulted in a much better accumulation in the cervical and brachial lymph nodes when compared to conventional liposomes. The accumulation in the liver was similar for both liposomal preparations, whereas an approximately twofold decrease in accumulation was observed for immunoliposomes in the spleen. Given that HLA-DR surface marker is expressed on monocyte/macrophages and activated CD4+ T lymphocytes, the primary cellular reservoirs of the human immunodeficiency virus (**HIV**), the use of liposomes bearing surface-attached anti-HLA-DR could constitute a convenient strategy to more efficiently treat this debilitating retroviral disease. Moreover, the reported incorporation of high amounts of host-encoded HLA-DR proteins by **HIV** particles renders the use of liposomes bearing anti-HLA-DR antibodies even more attractive.

L23 ANSWER 8 OF 16 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
1999:789929 The Genuine Article (R) Number: 245PW. **Targeting** lymph nodes with liposomes bearing anti-HLA-DR Fab' fragments. Dufresne I; **Desormeaux A**; BestmanSmith J; Gourde P; **Tremblay M J**; **Bergeron M G (Reprint).** UNIV LAVAL, CHU QUEBEC, CTR RES INFECT, PAVILLON CHUL, 2705 BLVD LAURIER, QUEBEC CITY, PQ G1V 4G2, CANADA (Reprint); UNIV LAVAL, CHU QUEBEC, CTR RES INFECT, QUEBEC CITY, PQ G1V 4G2, CANADA. BIOCHIMICA ET BIOPHYSICA ACTA-BIOMEMBRANES (15 OCT 1999) Vol. 1421, No. 2, pp. 284-294. Publisher: ELSEVIER SCIENCE BV. PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. ISSN: 0005-2736. Pub. country: CANADA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The ability of liposomes bearing anti-HLA-DR Fab' fragments to target cells expressing the human HLA-DR determinant of the major histocompatibility complex class II (MHC-II) has been evaluated and compared to that of conventional liposomes. Anti-HLA-DR immunoliposomes did not bind to HLA-DR-negative cells. In contrast, a high level of binding was observed following incubation of immunoliposomes with cells bearing important levels of human HLA-DR. The accumulation of conventional and murine anti-HLA-DR immunoliposomes in different tissues has been investigated following a single subcutaneous injection given in the upper

back of C3H mice. Anti-HLA-DR immunoliposomes resulted in a much better accumulation in the cervical and brachial lymph nodes when compared to conventional liposomes. The accumulation in the liver was similar for both liposomal preparations, whereas an approximately twofold decrease in accumulation was observed for immunoliposomes in the spleen. Given that HLA-DR surface marker is expressed on monocyte/macrophages and activated CD4+ T lymphocytes, the primary cellular reservoirs of the human immunodeficiency virus (**HIV**), the use of liposomes bearing surface-attached anti-PILE-DR could constitute a convenient strategy to more efficiently treat this debilitating retroviral disease. Moreover, the reported incorporation of high amounts of host-encoded HLA-DR proteins by **HIV** particles renders the use of liposomes bearing anti-HLA-DR antibodies even more attractive.

L23 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
1998:435776 Document No. 129:100037 Liposomes encapsulating antiviral drugs. **Bergeron, Michel G.**; **Desormeaux, Andre** (Bergeron, Michel G., Can.). U.S. US 5773027 A 19980630, 18 pp., Cont.-in-part of U. S. Ser. No. 316,735, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1995-538457 19951003. PRIORITY: US 1994-316735 19941003.

AB A method is disclosed for the treatment of viral diseases comprising the administration of antiviral agents encapsulated in liposomes. Also provided are formulations of liposomes for the treatment of viral diseases and more particularly for the treatment of infections caused by viruses like human immunodeficiency virus (**HIV**) and cytomegalovirus (CMV). These formulations of liposomes are composed of specific classes of lipid components and contain an entrapped drug effective against the viral disease. These liposomal formulations of antiviral drugs allow high cellular penetration in different cell lines, good in vitro antiviral efficacy against **HIV** and CMV replication, efficient in vivo **targeting** of **HIV** reservoirs and a marked improvement of the pharmacokinetics of drugs.

L23 ANSWER 10 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
1998:457623 Document No.: PREV199800457623. **Targeting** lymphoid tissues with liposomes. Bestman-Smith, J.; Gourde, P.; Dufresne, I.; **Desormeaux, A.**; Harvie, P.; **Tremblay, M. J.**; Beauchamp, D.; **Bergeron, M. G.**. Infection Dis. Res. Center, Centre Hospitalier Univ. Quebec, Pavillon CHUL, 2705 Boul. Laurier, Quebec City, PQ G1V 4G2, Canada. Journal of Liposome Research, (Feb., 1998) Vol. 8, No. 1, pp. 43-44. print.
Meeting Info.: Sixth Liposome Research Days Conference. Les Embiez, France. May 28-31, 1998.
ISSN: 0898-2104. Language: English.

L23 ANSWER 11 OF 16 MEDLINE on STN DUPLICATE 6
1998439953. PubMed ID: 9769017. Liposomes as drug delivery system: a strategic approach for the treatment of **HIV** infection. **Desormeaux A**; **Bergeron M G.** (Centre de Recherche en Infectiologie, Centre Hospitalier Universitaire de Quebec, Quebec, Canada.) Journal of drug targeting, (1998) 6 (1) 1-15. Ref: 105. Journal code: 9312476. ISSN: 1061-186X. Pub. country: Switzerland. Language: English.

AB As the number of individuals infected with human immunodeficiency virus (**HIV**) is growing dramatically throughout the world, it is important to develop strategies to improve the treatment of this deadly disease. It is now well established that macrophages play a central role in **HIV** pathogenesis, acting as reservoirs for dissemination of virus throughout the immune system. As liposomes are naturally taken up by cells of the mononuclear phagocytic system, liposome-based therapy represents a convenient approach to improve the delivery of anti-**HIV** agents into infected cells improving thereby the efficacy of drugs and reducing their adverse side-effects. A more specific **targeting** of **HIV**-infected cells could also be obtained by using liposomes bearing surface attached-antibodies. This review

details the applications of liposomes as drug carriers for the treatment of AIDS. It also gives an overlook of the different strategies that could be explored to control the progression of the disease in infected individuals.

L23 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
1996:404742 Document No. 125:67704 Liposome formulations for treatment of viral diseases. **Bergeron, Michel G.; Desormeaux, Andre** (Bergeron, Michel, G., Can.). PCT Int. Appl. WO 9610399 A1 19960411, 35 pp. DESIGNATED STATES: W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-CA561 19951003. PRIORITY: US 1994-316735 19941003.

AB A method is disclosed for the treatment of viral diseases comprising the administration of antiviral agents encapsulated in liposomes. Also provided are formulations of liposomes for the treatment of viral diseases and more particularly for the treatment of infections caused by viruses like human immunodeficiency virus (**HIV**) and cytomegalovirus (CMV). These formulations of liposomes are composed of specific classes of lipid components and contain an entrapped drug effective against the viral disease. These liposomal formulations of antiviral drugs allow high cellular penetration in different cell lines, good in vitro antiviral efficacy against **HIV** and CMV replication, efficient in vivo **targeting** of **HIV** reservoirs and a marked improvement of the pharmacokinetics of drugs.

L23 ANSWER 13 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
1996:400600 Document No.: PREV199699122956. **Targeting** lymphoid organs in **HIV** disease. Harvie, Pierrot [Reprint author]; Dusserre, N.; **Desormeaux, A.**; **Tremblay, M.**; Beauchamp, D.; **Bergeron, M. G.**. Cent. Recherche Infect., Cent. Hosp. l'Univ. Laval, Ste-Foy, PQ G1V 4G2, Canada. ELEVENTH INTERNATIONAL CONFERENCE ON AIDS. (1996) pp. 213. Eleventh International Conference on AIDS, Vol. Two. One world: One hope. Publisher: Eleventh International Conference on AIDS, Vancouver, British Columbia, Canada. Meeting Info.: Eleventh International Conference on AIDS, Vol. Two. One world: One hope. Vancouver, British Columbia, Canada. July 7-12, 1996. Language: English.

L23 ANSWER 14 OF 16 MEDLINE on STN
96002166. PubMed ID: 7549153. **Targeting HIV** with liposome-encapsulated antivirals. **Desormeaux A; Bergeron M G.** Zentralblatt fur Bakteriologie : international journal of medical microbiology, (1995 Apr) 282 (3) 225-31. Ref: 15. Journal code: 9203851. ISSN: 0934-8840. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

L23 ANSWER 15 OF 16 MEDLINE on STN DUPLICATE 7
96035232. PubMed ID: 7546414. Lymphoid tissues **targeting** of liposome-encapsulated 2',3'-dideoxyinosine. Harvie P; **Desormeaux A**; Gagne N; **Tremblay M**; Poulin L; Beauchamp D; **Bergeron M G.** (Centre de Recherche en Infectiologie, Centre Hospitalier de l'Universite Laval, Ste-Foy, Quebec, Canada.) AIDS (London, England), (1995 Jul) 9 (7) 701-7. Journal code: 8710219. ISSN: 0269-9370. Pub. country: United States. Language: English.

AB OBJECTIVE: To improve the pharmacokinetics and lymphoid tissues **targeting** of 2',3'-dideoxyinosine (ddI) by encapsulation in liposomes. METHODS: The pharmacokinetics and tissue distribution of free and liposome-encapsulated ddI were determined in C57BL/6 mice following intravenous and subcutaneous administration of a single bolus dose (3 mg ddI/kg). RESULTS: Intravenous administration of liposome-encapsulated ddI greatly reduced the systemic clearance of the anti-**HIV** agent.

The elimination plasma half-life of ddI incorporated in 112 and 83 nm liposomes was 46 and 14 times higher than that of the free drug, respectively. The tissue distribution profile of liposomal lipids clearly showed that the use of liposomes allows efficient **targeting** of lymph nodes and macrophage-rich tissues (spleen and liver) for at least 24 h following intravenous injection. In contrast, the accumulation of liposomes in these tissues was much lower following subcutaneous administration. CONCLUSION: Incorporation of ddI in liposomes greatly improved the pharmacokinetics of the anti-**HIV** agent after intravenous injection. The use of liposomes could represent a convenient approach to **targeting** lymphoid tissues. Strategies aimed at improving drug retention within liposomes should further enhance and prolong drug delivery to lymphoid organs.

L23 ANSWER 16 OF 16 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
95:316375 The Genuine Article (R) Number: QW052. **TARGETING HIV** WITH LIPOSOME-ENCAPSULATED ANTIVIRALS. **DESORMEAUX A (Reprint)**; **BERGERON M G.** UNIV LAVAL, CTR HOSP, CTR RECH, INFECTIOL LAB, 2705 BOUL LAURIER, LAVAL, PQ G1V 4G2, CANADA (Reprint); UNIV LAVAL, CTR HOSP, CTR RECH, SERV INFECTIOL, LAVAL, PQ G1V 4G2, CANADA; UNIV LAVAL, FAC MED, DEPT MICROBIOL, LAVAL, PQ G1V 4G2, CANADA. ZENTRALBLATT FUR BAKTERIOLOGIE-INTERNATIONAL JOURNAL OF MEDICAL MICROBIOLOGY VIROLOGY PARASITOLOGY AND INFECTIOUS DISEASES (APR 1995) Vol. 282, No. 3, pp. 225-231. ISSN: 0934-8840. Pub. country: CANADA. Language: ENGLISH.

=> s liposome encapsulated HLA
L24 0 LIPOSOME ENCAPSULATED HLA

=>

---Logging off of STN---

=>
Executing the logoff script...

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	520.88	521.15

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-89.67	-89.67

STN INTERNATIONAL LOGOFF AT 09:47:16 ON 09 AUG 2004